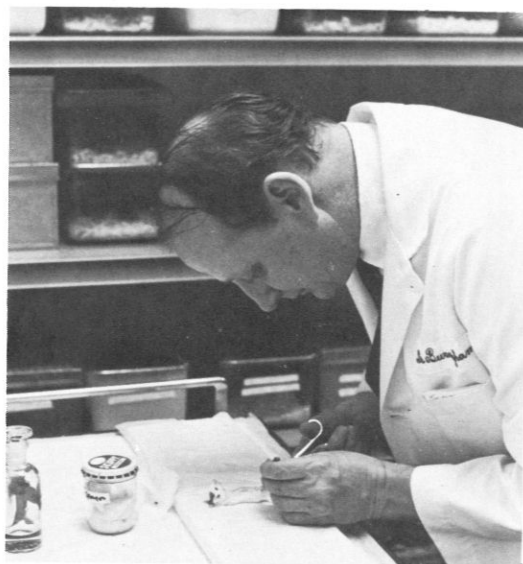
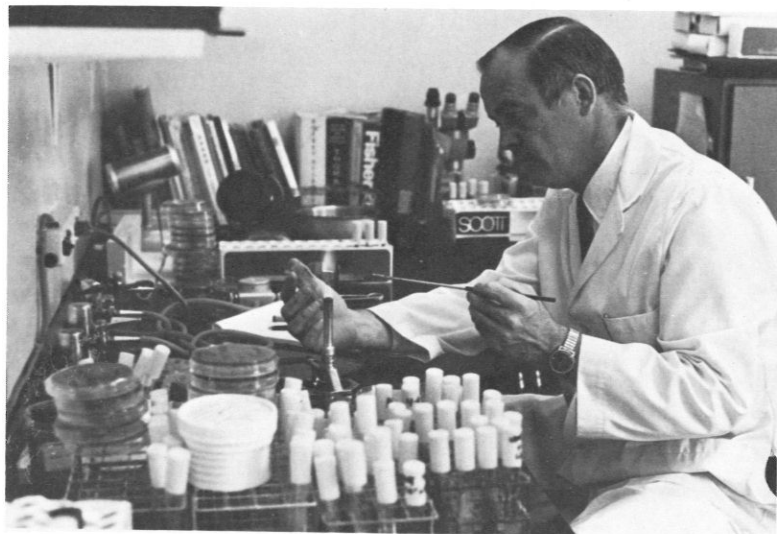




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NAVMED P-5088



from the Chief

This issue of U.S. NAVY MEDICINE represents the second annual publication of abstracts submitted by clinical and research investigators operating at naval hospitals throughout the U.S. An overall review of these progress reports will place in perspective the scope and objectives of the Clinical Investigation Program (CIP) and the military-mission-oriented Research, Development, Testing and Evaluation (RDT&E) program.

Charged with establishing priorities in the face of limited staff and funds, many clinicians would plead that their uppermost objective is to render quality patient care. I have no argument with that. It remains equally true, however, that better and more efficient patient care is not a stationary operation. An inquiring mind and well-disciplined efforts to better define or improve our methods of health care delivery are essential to meet the professional demands of quality patient care.

It is my conviction that those in the best position to dictate appropriate standards and professional requirements are those who regard patient care as their prime purpose. If this be so, then it naturally follows that dedicated clinicians would be ill advised to divorce and excuse themselves from involvement in present research and clinical investigation activity.

Participation by all of our staff members in, or in conjunction with suitable naval medical facilities is mandatory if our professional competence is to continue and advance. In a very real sense, the degree to which we exert effort in research and clinical investigation will ultimately determine the viability of our Medical Corps and the quality of our performance.



From the Assistant Chief For Research and Military Medical Specialties

RADM P.O. Geib, MC, USN

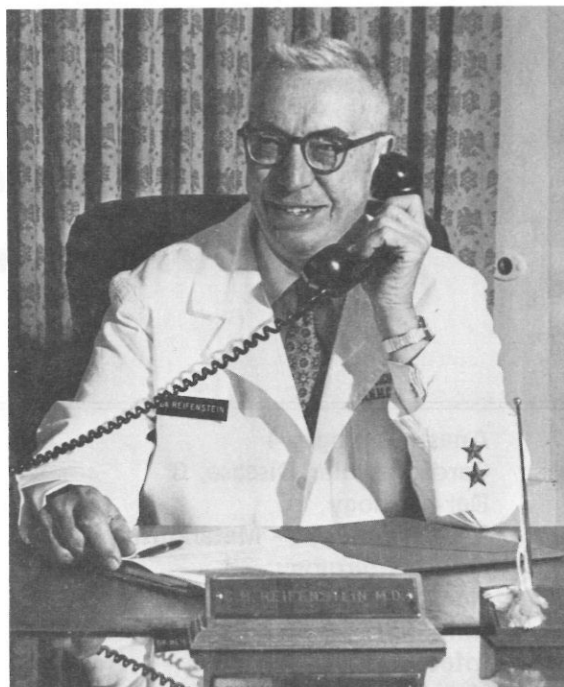


The Research Division of the Bureau of Medicine and Surgery welcomes this opportunity to present the abstracts of research performed at naval hospitals throughout the United States.

Navy medical research is primarily directed toward answering problems which are related to the health maintenance and care of the operating forces of the Navy and Marine Corps. The major effort is conducted within the Research, Development, Test and Evaluation (RDT&E) activities under the command of the Chief, Bureau of Medicine and Surgery. A very important effort is the clinically oriented research and development work in the naval hospitals. The funding of well designed and militarily relevant research tasks in naval hospitals will be continued. The combination of Research Program and Clinical Investigation Program efforts will support and encourage a high level of professional competence and scientific interest in naval hospital staffs.

From the Director, CICC*

RADM George H. Reifenstein, MC, USNR



This is the second annual CIP† and RDT&E†† issue of U.S. NAVY MEDICINE, which emphasizes continuing progress in the Navy Medical Department's clinical investigation accomplishments.

The CIP Directive (BUMED INSTRUCTION 6000.4A) has been revised since the last CIP/RDT&E issue. Among the major changes within this directive are simplified and specific submission, progress and termination procedures, and a guideline check-off sheet enclosure. In our larger hospitals with designated Clinical Investigation Centers, provision is also made, through the submission of certain management and technical reports to provide overhead and other support to the activity Clinical Investigation Centers.

Important advances in clinical investigation and clinical research are evidenced in the abstracts included in this issue. CIP abstracts, identified by a CICC number, are selected from progress reports submitted annually on 1 Feb. All approved clinical investigation studies for which scientific data have been submitted to CICC are included within this issue.

In keeping with our initial presentation in the Jun 1972 issue of U.S. NAV MED, classification of studies into subsections has been based on content rather than the originating department. An alphabetical index of investigators, with subsection and page references follows the abstracts.

The vitality of clinical investigation and research are maintained through close communication between the investigator and CICC (by progress reports, abstracts and correspondence) through travel by the CICC director and his administrative officer to hospital research areas, and close coordination with the various RDT&E codes within BUMED. While visits to the field must be generally restricted to those hospitals with designated Clinical Investigation Review Centers (CIRCs), interested physicians and investigators from other Naval medical facilities should feel free to communicate through channels, with the CICC Director, on specific aspects of a clinical investigation proposal or approved study.

As before and in keeping with the policy of the Editor of U.S. NAVY MEDICINE and Director, CICC, specific comments are welcome. BUMED CICC (Code 10) is located in Tower 18, National Naval Medical Center, Bethesda, Maryland 20014; telephone (202) 295-0584, autovon 295-0584-0585.

*CICC = Clinical Investigation Control Center

†CIP = Clinical Investigation Program

††RDT&E = Research, Development, Test and Evaluation

CIP and RDT&E

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ANESTHESIOLOGY

MODIFICATION OF HALOTHANE EFFECTS ON ATRIO-VENTRICULAR (A-V) CONDUCTION BY LIDOCAINE AND DIPHENYLHYDANTOIN. J.L. Atlee and R.E. Tobey. Naval Hospital, Bethesda.

Halothane has been shown in studies employing His bundle electrograms to depress A-V conduction in dogs. Impaired A-V conduction may contribute to arrhythmias during anesthesia and operation, as may enhanced automaticity. Lidocaine and diphenylhydantoin both decrease automaticity and in therapeutic concentrations improve conductivity. In the present experiment lidocaine and diphenylhydantoin either improve or minimally influence A-V conduction impaired by halothane. These results suggest that lidocaine and diphenylhydantoin may be of value in treating cardiac arrhythmias during halothane anesthesia.

(The authors gratefully acknowledge the use of the facilities at the Armed Forces Radiobiological Research Institute in carrying out these experiments.)

CICC 2-06-321

RENAL FUNCTION AND METHOXYFLURANE ANESTHESIA: A CLINICAL STUDY. J.H.J. Brown, D.A. John, V.C. Lanier and R.E. Tobey. Naval Hospital, Bethesda.

Recent reports have implicated methoxyflurane anesthesia with the development of postoperative high output renal disease. These reports have indicated that the pathology is dose related, and that the causative factor may be the concentration of fluoride ion released by the metabolism of the agent. To date, 16 out of an anticipated 20 studies have been completed. Our preliminary findings support the data reported in other papers indicating that methoxyflurane produces no clinical or laboratory evidence of renal toxicity and is a safe anesthetic agent, if a predetermined, low-dosage administration schedule is strictly followed. CICC 2-06-318

APNEIC OXYGENATION IN ANESTHESIA. H. Dean, J.L. Steffenson, L.A. Sheffer and R.L. Fraioli. Naval Hospital, Oakland.

The technique of apneic oxygenation (supplying

oxygen to the upper airway of patients who are not breathing) has long been used in anesthesia for various types of surgical procedures such as direct laryngoscopy, tonsillectomy and bronchoscopy. Many studies investigating the respiratory and cardiovascular effects of this technique have been done and valuable information obtained.

Although apneic oxygenation is a useful technique in anesthesia, it no doubt could be made more useful if more were known about it. For example, what happens to the P_{aO_2} (partial pressure of oxygen in arterial blood) after five minutes? (In 1963 Heller studied P_{aO_2} values obtained only over a five-minute period.) What changes in shunt fractions and FRC (functional residual capacity) do occur and how much do they influence the P_{aO_2} ? What are the differences between using an airtight nasotracheal catheter and a simple nasal catheter to supply 100% O_2 to the lower airway? How is oxygen inflow from a reservoir quantitatively related to O_2 diffusion into the blood? What are the limitations of the technique of apneic oxygenation? MR041.20.01-4001

PULMONARY AND CARDIOVASCULAR EFFECTS OF APNEIC OXYGENATION IN HUMANS. R.L.

Fraioli, L.A. Sheffer and J.L. Steffenson. Naval Hospital, Oakland.

Apneic oxygenation was studied in 13 patients undergoing Jakolaryngoscopy with a pharyngeal catheter for oxygen administration and 18 patients having minor surgical procedures using a cuffed endotracheal tube in place for oxygen administration. Changes were observed in P_{aO_2} (partial pressure of oxygen in arterial blood), P_{aCO_2} (arterial CO_2 tension) and pH (the negative logarithm of hydrogen ion concentration), FRC (functional residual capacity), P_{AN_2} (PN_2 of alveolar gas), oxygen inflow, arterial blood pressure, and electrocardiogram. Comparison of the two methods of oxygen administration revealed essentially no difference between them with the majority of patients tolerating apneic oxygenation for 15 minutes or longer. There were patients with both methods, however, who could not tolerate apneic oxygenation for more than 5 minutes. Analysis of the data revealed that those patients who could not tolerate apneic oxygenation had relatively smaller FRCs and larger body mass, or an FRC/weight ratio of 13.0 ± 2.4 cc/kg; whereas, the others had an FRC/wt ratio of 23.0 ± 5.8 cc/kg. Because of the smaller FRC and larger body mass accumulating alveolar nitrogen resulted in a higher P_{AN_2}

and a lower P_{AO_2} (PO_2 of alveolar gas) in those patients with a low FRC/wt ratio.

CICC 2-48-202

EFFECT OF ANESTHESIA ON OXYGEN-CARRYING CAPACITY OF BLOOD. M.S. Jakubowski, S.V.

Vescera, L.T. York and C.R. Valeri. Naval Hospital Boston, Chelsea, Mass.

This study was undertaken to determine the effect of halothane and general anesthesia on restoration of oxygen-carrying capacity of stored blood. ACD blood stored for 21 days was rejuvenated with a medium consisting of pyruvate, inosine, glucose and phosphate to restore red cell 2,3-DPG (diphosphoglycerate) and ATP (adenosine triphosphate) to normal. Restoration of red cell P_{50} by this medium, *in vitro*, was not inhibited by halothane. *In vivo* studies are in progress on patients transfused intra-operatively. Following a four-unit transfusion of stored blood, the red cell 2,3-DPG and P_{50} (partial pressure of oxygen at which the hemoglobin is 50% saturated) are significantly lowered. The values are restored to normal in 24-48 hours; general anesthesia does not alter this restoration.

CICC 2-02-109

EFFECT OF ANESTHESIA ON BLOOD COAGULATION. M.S. Jakubowski, S.V. Vescera, L.T. York and

C.R. Valeri. Naval Hospital Boston, Chelsea, Mass.

In approaching the effect of anesthesia on blood coagulation, the first step has been a study of the effect of halothane on platelet aggregation. The data showed that halothane vapor 1.7%, equilibrated with whole blood or platelet-rich plasma, retarded platelet aggregation induced *in vitro* by *l*-epinephrine or adenosine diphosphate. This effect was reversible by "halothane washout." Physical damage to platelets, as a mechanism for this effect, was ruled out by morphological studies and the hypotonic stress test.

CICC 2-02-115

THE INFLUENCE OF ENZYME INDUCTION ON TRICHLOROETHYLENE ANESTHESIA. J.M. Kelley.

Naval Hospital, Bethesda.

Anesthetic effects of trichloroethylene will be studied in experimental animals which have been pretreated with a known inducer of liver microsomal enzymes, phenobarbital, to find out if enhanced metabolism of trichloroethylene decreases sleeping time following anesthesia. Trichloroethylene and its metabolites with hypnotic activity, chloral hydrate and trichloroethanol,

will be measured by gas chromatography. An inactive metabolite, trichloroacetic acid, will be measured by the Fujiwara reaction. Preliminary study suggests that although no change in sleeping time exists, animals which have received phenobarbital have less trichloroethylene, and more chloral hydrate and trichloroethanol in their blood at the time of awakening from anesthesia than do control animals. The results of this study will clarify the mechanism of trichloroethylene anesthesia.

CICC 3-06-192

EFFECT OF OSMOTIC DIURESIS ON DURATION OF NEUROMUSCULAR BLOCKADE INDUCED BY NON-DEPOLARIZING MUSCLE RELAXANTS.

B.M. Rigor and W.M. McDermott. Naval Hospital, Portsmouth, Va.

Osmotic diuresis is sometimes necessary during anesthesia involving the use of the non-depolarizing muscle relaxants, curare and gallamine.

As the excretion of these drugs is predominantly by renal mechanisms, it is postulated that this diuresis might significantly shorten their duration of action.

Currently, under barbiturate anesthesia and controlled ventilation, curare or gallamine is being administered to cats and the magnitude and duration of paralysis is being measured. At a later date, adding mannitol to the regimen, the procedure will be repeated on the same animal.

CICC 2-08-502

RECOVERY ROOM ANALGESIA: A COMPARATIVE STUDY OF DRUG EFFECTS. **L.A. Sheffer and H.N. Dean.** Naval Hospital, Oakland.

The recovery-room condition of pediatric patients undergoing tonsillectomy with nitrous oxide-halothane anesthesia was evaluated by two parameters: alertness and tranquility. Patients were given an intramuscular injection of a study drug 15 minutes prior to the end of anesthesia. Drugs studied were: placebo (normal saline), hydroxyzine, diazepam, fentanyl, ketamine at 2-dose levels, and meperidine. Results have shown distinct differences between drugs which are consistent, indicating that our method of evaluation is good. We have shown that the administration of analgesic drugs close to the end of anesthesia is effective in producing a quiet, comfortable patient in the recovery room. Of the drugs tested meperidine, 1 mgm/kg, has been found to be most desirable on the basis of smooth, rapid

recovery of alertness with good tranquility and a low incidence of side effects.

CICC 3-48-095

A STUDY OF CARBON MONOXIDE PRODUCTION DURING ANESTHESIA AS A METHOD OF DETERMINING RED BLOOD CELL HEMOLYSIS AND RED BLOOD CELL SURVIVAL. **S. Vescera.** Naval Hospital Boston, Chelsea, Mass.

This study is designed to evaluate the red cell mass and turnover in the patient subjected to surgical stress. Carbon monoxide is a product of hemoglobin breakdown and by placing the patient in a closed breathing circuit to prevent respiratory excretion, the carbon monoxide can be used to calculate the hemoglobin mass and turnover.

To date, 21 studies have been completed; 14 have yielded measurable hemoglobin mass and turnover rates; the other seven studies were eliminated because of technical problems early in the study. Chromium red cell masses have been done simultaneously in 11 of these studies.

The relationship between the carbon monoxide space (CO binding capacity of blood) and the hemoglobin mass measured by the chromium method is $1.40 \times \text{Hgb(gm)} - 60.18$ ($p < 0.01$). The slope of the line is comparable to the theoretical slope of 1.39.

CICC 3-02-060

CARDIOVASCULAR DISEASE

EVALUATION OF THE EFFECTS OF ACUTE INFARCTECTOMY ON POST-INFARCT ARRHYTHMIAS. **Benjamin L. Aaron and William Hix.** Naval Hospital, Portsmouth, Va.

The effect of excision of acutely infarcted areas of myocardium upon control or relief of intractable arrhythmias is to be evaluated.

An experimental dog model will be used with documentation of the extent of infarction, type and responsiveness of arrhythmias to standard treatment followed by infarctectomy for intractable arrhythmias. Pertinent parameters are the further course of the arrhythmia(s) and survival from the acute infarction.

Six dogs have been included in the study thus far. Of the six, only two developed refractory arrhythmia. Following excision of the infarcts the arrhythmia disappeared, and strong, effective contraction and cardiac output ensued. Four of the six developed acute

aneurysmal paradox of the left ventricle with inability to maintain a satisfactory arterial pressure. Resection of the atonic infarcted area resulted in strong, effective contraction and cardiac output.

The numbers are small but the postulate that resection of the injured muscle improves immediate cardiac function is supported by the early results.

CICC 2-08-511

LONGITUDINAL STUDY OF CORONARY ARTERY DISEASE AND MYOCARDIAL REVASCULARIZATION SURGERY. William P. Baker. Naval Hospital, Bethesda.

This program is designed to study the relationship of angiographic data to the subsequent clinical course in unoperated patients with coronary heart disease and to note the influence of saphenous vein bypass graft surgery on the clinical course in operated cases. These data will be used to establish more adequate criteria for surgery.

Approximately 200 cases of coronary artery disease have undergone clinical evaluation and cineangiographic confirmation. Eighty-five patients have received one or more saphenous vein bypass grafts and about 45 of these patients have been restudied. Cases continue to be added to the study at a rate of five to ten per month. It is anticipated that an analysis of these data after another year will yield valuable information relevant to surgical mortality, graft patency rate, and the influence of surgery on symptomatic classification. Limited observations on the influence of severity and location of obstructive lesions on subsequent clinical course in the unoperated group will be possible after a somewhat longer period of observation.

CICC 2-06-315

LONG-TERM OBSERVATIONS IN PATIENTS WITH ANGINA AND NORMAL CORONARY ARTERIOGRAMS. C.R. Bemiller, C.J. Pepine and A.K. Rogers. Naval Hospital, Philadelphia.

Thirty-seven patients (mean age 42.7 years) with angina pectoris (AP), ischemic myocardial abnormalities and normal coronary arteriograms were followed for 4.1 years (mean). Twenty patients had typical and 17 atypical AP. Ten had normal serum lipids; eight had abnormal glucose tolerance tests. Rest-to-exercise hemodynamics revealed increased left ventricular (LV) end-diastolic pressure (mean 11.2 ± 2.6 mmHg \rightarrow 19.1 ± 3.6 , $p < 0.05$), while stroke work index increased (+29%). LV ischemia was detected by abnormal lactate extraction with atrial pacing in ten patients,

or by a 1 mm (or more) S-T segment depression during exercise or pacing in 27 patients.

After a mean follow-up period of 4.1 years, AP decreased in 80% of cases, and remained stable in the other 20%. One patient died suddenly and autopsy revealed normal coronary arteries and myocardium. In the remainder, complications of ischemia, i.e. progression of symptoms, infarction and heart failure were absent. Seven patients, restudied 4.5 years (mean) later, had no changes in their previously documented hemodynamic abnormalities and normal coronary arteriograms.

The fate of patients with AP and normal coronaries with ischemic LV abnormalities (ECG, metabolic, or hemodynamic) appears favorable. AP responds to nitrate and propranolol therapy. These long-term clinical observations with repeated angiographic and hemodynamic studies suggest a nonprogressive disorder.

MR041.20.01-0132

ALTERATIONS IN RENAL CLEARANCE OF DIGOXIN. D.D. Brown. Naval Hospital, Pensacola.

This investigation, using hospitalized patients and a radioimmunoassay for measuring plasma and urinary digoxin concentrations, should delineate the changes in the ratio of digoxin renal clearance to urea and creatinine clearances produced by such interventions as diuresis with furosemide.

Preliminary data has characterized the cross reactivity of the antibody system with the various urinary metabolites of digoxin.

Data from the few patients studied to date demonstrate the ease and feasibility of digoxin renal clearance determinations and indicate that the digoxin clearance is going to lie between 60 to 100% of the creatinine clearance.

CICC 2-08-525

ALLOGENEIC LYOPHILIZED VENOUS GRAFTS AS RENAL ARTERY SUBSTITUTES IN COMBAT-INDUCED TRAUMA. N.L. Constantinople and P.C. Walsh. Naval Hospital, San Diego.

This study is designed to evaluate the feasibility of a new vascular graft, allogeneic lyophilized saphenous vein, in the replacement of traumatized renal vasculature. Its performance and patency will be compared to two more widely used grafts: autogenous saphenous vein and the bovine-carotid, tanned-collagen prosthesis. Ability of the grafts to withstand various stresses, including an atherogenic regimen, will also be investigated.

Under sterile technique, allogeneic canine saphenous vein segments will be procured, frozen and lyophilized in the facilities at Tissue Bank, West, Naval Hospital San Diego. These segments will be implanted as renal artery substitutes in dogs. Bovine, tanned-collagen, arterial prostheses and autogenous saphenous veins will be implanted in the contralateral renal artery. Renal function and patency of the grafts will be evaluated at intervals by excretory urography and renal angiography. To further examine the long-term degenerative responses of the graft, one-half of the dogs will be placed on an atherogenic diet for six months. After sacrifice, various studies will be performed to evaluate the responses of the varying grafts to this stress.

Twelve dogs have been operated upon. Six out of the last seven have survived; the first two IVPs and renal angiograms performed at six weeks revealed function of the grafted kidneys and patency of the lyophilized grafts. Four to six more animals will be grafted before initiating the diet regimen.

M4305.03-3021

THE DIAGNOSIS OF PERICARDITIS SECONDARY TO MENINGOCOCCAL DISEASE IN MILITARY PERSONNEL BY ELECTROCARDIOGRAPHIC MAPPING. D.M. Davidson and A.D. Hagan. Naval Hospital, San Diego.

Meningococcal meningitis and meningococcemia and their complications continue to be a significant problem for the military services. Recent investigation has shown a higher incidence of pericarditis than was previously supposed. An accurate, non-invasive method of determining the myocardial injury associated with meningococcal disease is needed, to facilitate prompt institution of appropriate treatment. Maroko and co-workers have devised a 35-lead precordial mapping device which offers a simple non-invasive method for quantitating myocardial injury. An objective, prospective study utilizing this device offers the promise of earlier and more accurate diagnosing of myocardial involvement.

All patients admitted to Naval Hospital San Diego, with a confirmed or suspected diagnosis of meningococcal meningitis or meningococcemia will be included in this study. Initial clinical evaluation will include baseline analysis of ST segment and T wave changes from normal, in addition to standard clinical measurements and monitoring for patients with meningococcal disease.

Due to the effectiveness of Group C Vaccine, only two patients admitted to this hospital were selected for study. One patient developed pericarditis; evidence of

pericarditis was evident by routine electrocardiogram before becoming manifest by auscultation or 12-lead electrocardiographic studies, thus allowing early treatment and careful observation of the response to medication.

M4305.05-3086

EVALUATION OF ROUTINE STRIP CHART RECORDING OF ECHOCARDIOGRAMS ON NEWBORNS AS AN AID IN DIAGNOSIS OF CONGENITAL CARDIAC ABNORMALITIES. W.J. Deely, M.A. Woodall, A.D. Hagan and J.R. Morgan. Naval Hospital, San Diego.

Electrocardiography, although a relatively recent innovation holds promise of great usefulness in the small subject since it is a non-invasive and benign procedure. However, experience needs to be gained in order to adequately define the relationship of the aortic and pulmonic valves, and the size and position of the ventricular septum in various defects.

To date, approximately 170 normal newborn infants have been studied by the ultrasound technique in an effort to establish and confirm normal values for chamber size, valve motion (speed and length of excursion) and valve size. Roughly 20-30 infants have had follow-up studies conducted several days after the initial study, to see if changing hemodynamics at this stage can be correlated with echocardiographic findings. Present progress is good and our plans call for a continuation of this present collection of normal newborn data, as well as an extension to include all neonates suspected of having cardiovascular abnormalities.

In the near future we plan to get serial recordings, from within the first few minutes and hours of life through 24 hours of age, to investigate the possibility of meaningful echocardiographic-hemodynamic correlations at this stage of life.

CICC 3-16-033

ANGIOGRAPHIC ANALYSIS OF LEFT VENTRICULAR MECHANICS IN YOUNG PATIENTS WITH ATYPICAL CHEST PAIN AND ISCHEMIC HEART DISEASE. G.F. Francis, J.R. Morgan and A.D. Hagan. Naval Hospital, San Diego.

Young patients being evaluated for suspected ischemic heart disease by the cardiology service at this hospital will be subjected to a thorough analysis of ventricular function by such methods as cardiac catheterization and angiography, as well as standard clinical and laboratory parameters for evaluation of such pathology. Abnormalities of left ventricular mechanics will be

carefully studied in those subjects with normal coronary arteriograms in an effort to identify the most significant parameters for the recognition of impaired left ventricular function.

We are now evaluating patients with the system. We have not examined enough patients to demonstrate significant trends.

MR041.20.01-0379

DIAGNOSIS AND TREATMENT OF VASCULAR DISEASE IN NAVAL PERSONNEL. W. Gee. Naval Hospital, Oakland.

To provide improved monitoring of cerebral blood flow in the casualty undergoing operation for carotid artery injury or brain trauma, it is planned to evaluate the effectiveness of ocular plethysmography. A total of 15 clinical cases have been studied with excellent correlation with angiographic findings. When the intracranial pressure transducer is available, ocular pulse waves with variations in intracranial pressure will be studied.

MR041.20.01-0262

EVOLUTION OF THE VECTORCARDIOGRAM IN THE NEWBORN INFANT. A.J. Griffin. Naval Hospital, Great Lakes.

Evolution of the vectorcardiogram in the newborn period has not been adequately established. Equipment has been obtained to initiate a study of electrocardiograms at four-hour intervals in the newborn period. Training of technicians on the equipment has been initiated.

To date, the data collected have been insufficient for analysis. In a single instance, however, the equipment has been of significant help in diagnosing a critically ill infant.

CICC 3-13-162

THE EFFECT OF PLURONIC F-68 ON CARDIOVASCULAR MECHANICS, REGIONAL BLOOD FLOW AND SMALL VESSEL PATENCY. F.L. Grover, J.R. Warden and B.F. Gibbs. Naval Hospital, San Diego.

Sixteen dogs (8 control and 8 experimental) were subjected to experimental hemorrhagic shock. Arterial pressure, central venous pressure, pulmonary artery pressure, pulmonary artery wedge pressure, heart rate, peripheral resistance, pulmonary vascular resistance, stroke volume, left ventricular stroke work, left ventricular work, carotid artery flow, and renal artery flow were determined prior to and immediately after

hemorrhage, and after the intravenous administration of 1 ml per kg of normal saline to the control group, and 1 ml per kg of 5% Pluronic F-68 to the experimental group. A significant increase in renal artery flow was found in the Pluronic group as compared to the control group. There was no significant difference between the experimental groups and the control groups in the other parameters measured.

Pluronic F-68 has been previously shown to increase the microcirculation in the mesentery and to increase survival in experimental hemorrhagic shock. These effects are apparently not related to an inotropic effect of the agent, but to its peripheral rheological properties. The effect of Pluronic F-68 on blood flow to other regions of the body needs to be determined as well as its effect on cardiac output and central circulatory dynamics, when given in conjunction with volume expansion.

MR041.20.01.0376

RADIOIMMUNOASSAY OF SERUM DIGOXIN LEVELS IN PATIENTS WITH ACUTE AND CHRONIC ARRHYTHMIAS AND POSTOPERATIVE CARDIAC SURGERY. A.D. Hagan and W.V.R. Vieweg. Naval Hospital, San Diego.

Digoxin levels will be compared in three related groups of patients with arrhythmias: (1) those with coronary artery disease and/or valvular heart disease, (2) those with clinical digitalis toxicity, and (3) those undergoing cardiac surgery who develop postoperative arrhythmias. Originally, 100 patients were to be selected for investigation over an 18-month period. However, this protocol has not been implemented due to an inability to perform serum digoxin levels at Naval Hospital, San Diego. Instead, a collaborative study has been implemented at University Hospital, San Diego, and the digoxin levels will be performed there. Modifications of the protocol are planned, to include two groups of patients with chronic atrial fibrillation of differing etiologies, coronary heart disease and rheumatic heart disease.

CICC 3-16-052

SYSTEMIC AND RENAL HEMODYNAMICS IN SALT-RETAINING STATES BEFORE AND AFTER THERAPY. Michael H. Humphreys and G. John Weir. Naval Hospital, Great Lakes.

Alterations in systemic and renal hemodynamics are known to occur in patients with cirrhosis and congestive heart failure who are retaining sodium. The simple bedside measurement of cardiac output, GFR

(glomerular filtration rate) and renal blood flow could conceivably contribute to the management of these disorders, as well as shed light on the underlying pathogenetic alterations.

Attempts have been made to measure cardiac output using isotopic injection and external counting with a precordial probe. However, agreement between this method and conventional dye-dilution techniques has not been good, chiefly because of the poor curve obtained for analysis using the precordial probe. Further refinements in technique are necessary before this could become a reliable and simple procedure.
CICC 2-13-015

MEASUREMENT OF PRA (PLASMA RENIN ACTIVITY) IN PATIENTS WITH HYPERTENSION. Michael H. Humphreys and Robert W. Spath. Naval Hospital, Great Lakes.

Recent attention has focused on that group of hypertensive patients with low circulating PRA, since a number of studies have implicated excessive mineralocorticoid production as being causally related to the hypertension. Work to date on this problem at this facility has involved the standardization of a commercially available kit for measurement of plasma renin by radioimmunoassay of angiotension I (E.R. Squibb and Sons, Inc). Random measurements of PRA, without attention to salt intake show values between 0.4 and 1.5 ngA-I/ml/hr, values too low to discriminate between normal and low-PRA hypertensive patients. When dietary salt is restricted and a thiazide diuretic is given for three days, mean PRA increases to 1.9 ng/ml/hr (normal = 3 ng/ml/hr) in normal subjects. The well-known increase in PRA following assumption of upright posture is also detected using this kit.

Once standardization of the assay procedure is completed, hypertensive patients will be screened for PRA using the standard low-salt diet and diuretic protocol.
CICC 3-13-141

INVESTIGATION OF CHEST PAIN AND PALPITATIONS IN ACTIVE DUTY PATIENTS WITH PROLAPSED MITRAL LEAFLET USING NON-INVASIVE TECHNIQUES. D.J. MacNeil and A.D. Hagan. Naval Hospital, San Diego.

Prolapsed posterior mitral leaflet is a common problem affecting young to middle-aged men and women which has only been clinically recognized during the past few years. This group presents a significant amount of chest complaints that were heretofore considered noncardiac or psychosomatic in origin.

Typically, these patients manifest variable apical systolic murmurs which are often confused with innocent murmurs. There is usually an associated mid-to-late systolic click. The degree of associated mitral regurgitation is generally of no hemodynamic significance, but the etiology of the atypical chest pain and palpitations has not been explained.

After clinical evaluation has excluded other possible causes of chest pain and extrasystoles; and after the diagnosis of prolapsed posterior mitral leaflet has been established by physical examination, phonocardiogram, echocardiogram, and coronary arteriograms when clinically indicated; the following parameters will be investigated: (1) resting phonocardiogram, systolic time intervals, apex cardiogram, and echocardiogram; (2) repeated evaluation of above procedures following amyl nitrate inhalation, hand grip dynamometer, IV phenylephrine infusion to increase after load, and intravenous Isuprel infusion; and (3) observation of the onset and disappearance of pain and ectopic beats with electrocardiograph monitoring throughout the procedures.
CICC 3-16-158

INTERMEDIATE CORONARY CARE: AN ANALYSIS OF IMPROVED SURVIVAL IN THE TREATMENT OF ACUTE MYOCARDIAL INFARCTION. A.L. Mattern, A.D. Hagan and J.R. Morgan. Naval Hospital, San Diego.

Analysis of effectiveness of intermediate coronary care units in reducing mortality rates in acute myocardial infarction is needed. Retrospective review of medical records of all patients hospitalized from 1969 to 1972, to determine mortality rate and causes of death in and out of the coronary care unit is being conducted. A twelve-month prospective study of the effect of intermediate coronary-care monitoring on survival rates in acute myocardial infarction, and the causes of death and percent survivors as compared to the previous 36-month period, is planned. Preliminary review of hospital records for a 36-month period from 1969-1972 has commenced, to determine mortality rates, cause of death, place of death and therapy.
CICC 3-16-164

MYOCARDIAL REVASCULARIZATION FOR ISCHEMIC HEART DISEASE. M. Mills and H.E. Ashworth. Naval Hospital, Bethesda.

We will determine if myocardial revascularization will relieve angina pectoris in patients with coronary atherosclerosis. An operation using saphenous vein bypass

grafts from the aorta to the coronary arteries is performed on selected patients.

To 31 Dec 1972, 75 myocardial revascularization procedures have been performed. There have been four operative deaths (within one month of operation) for a mortality rate of 5.3%. To date, 39 patients have been restudied. Twenty patients had single coronary artery bypass grafts and 80% of these are patent. Fourteen patients had double grafts. Fifty-seven percent of the 28 grafts are patent and 85.7% of these patients have at least one graft patent. Five patients had triple grafts. Only 33.3% of these 15 grafts are open but 60% of these patients have at least one graft patent. Of those patients restudied, 66% are free of angina, another 8% have had improvement in their angina and 26% are unimproved. There has been one late death (1.3%). Of the 75 patients, 24 (32%) have been on active duty and 13 (54%) of these have been returned to full duty.

Myocardial revascularization has a low operative mortality and significant symptomatic improvement is obtained in a high percentage of patients.
CICC 2-16-316

DETECTION OF OCCULT VENOUS THROMBOSIS BY AN IMPEDANCE METER AND ¹²⁵I FIBRINOGEN. Robert L. Mullin and H. William Fegley. Naval Hospital Boston, Chelsea, Mass.

The purpose of this study is to evaluate the Codman Impedance Phlebograph machine in detecting occult venous thrombosis. Thus far 201 patients have been examined; 453 phlebograph studies have been done, of which 105 (or approximately 23%) were abnormal. About 10% of the studies were followed by venography and a good correlation was found. Enough confidence has now been established in the Impedance Phlebograph apparatus to treat, or not treat patients with anticoagulation on the basis of the phlebograph tracings alone.
CICC 2-02-101

PREVENTION OF POSTOPERATIVE VENOUS THROMBOSIS BY ASPIRIN, DEXTRAN, COUMADIN AND INTERMITTENT COMPRESSION UNIT. R.L. Mullin and H.W. Fegley. Naval Hospital Boston, Chelsea, Mass.

The purpose of this study is to investigate the effect of various therapeutic modalities on the incidence of venous thrombosis and pulmonary emboli. "High risk" elective surgical patients will be randomized into therapy groups: (1) aspirin treated, (2) dextran treated,

(3) Coumadin treated, (4) intermittent extremity compression and (5) control. The patients will be evaluated using the impedance phlebograph apparatus.
CICC 2-02-102

BEDSIDE STUDY OF CVP AND WEDGE PRESSURE IN ACUTE MYOCARDIAL INFARCTION. H.J. Palay and R. Landesman. Naval Hospital, Great Lakes.

The often noted disparity between left and right heart filling pressures in acute myocardial infarction is being studied using a double-lumen, Swan-Ganz catheter. In addition, wedge pressure (pulmonary artery diastolic pressure) is being correlated with the magnitude of the p-terminal force in V1 in patients with congestive failure and pulmonary edema.

At this date insufficient patients have been studied to reach a valid conclusion.
CICC 2-13-011

EVALUATION OF THE CARDIOVASCULAR AND ANTI-ANGINAL EFFECTS OF MIXIDINE. C.J. Pepine. Naval Hospital, Philadelphia.

Recently completed bioviability studies have shown only 30% absorption of salt currently in investigational use. This information suggests that very large doses (> 1,200 mg/day) will be needed to achieve a physiologic effect and even larger doses may be required to demonstrate an anti-anginal action. Presently the intravenous form is being reevaluated and a new oral form is being manufactured. Because it is impractical to administer these potentially large doses in a clinical setting and it is likely that a new form of Mixidine will replace the current oral preparation, work on this project has been postponed.
CICC 3-05-064

THE FUNCTIONAL SIGNIFICANCE OF IMPAIRED CARBOHYDRATE TOLERANCE (DIAB) IN PATIENTS WITH CORONARY HEART DISEASE (CHD). C.J. Pepine and C.R. Bemiller. Naval Hospital, Philadelphia.

The functional significance of DIAB with CHD was investigated in 18 patients. Resting and exercise left ventricular (LV) and systemic pressures, LV work index (LVWI), and heart rate (HR) were determined in addition to selective coronary angiography (scored - 1 point/lesion 50% obstruction).

Symptomatic (Class II and III) diabetic patients had similar coronary angiographic scores (mean, 2.3/patient) compared to symptom-matched, age-matched

non-DIABs (2.1/patient), and the frequency of demonstrable inter-coronary collateral vessels was similar (39% of DIABs vs 35% of non-DIABs). Absence of DIAB appeared to afford protection against LV hemodynamic abnormalities as exercise LV end-diastolic pressure increased more (DIABs vs non-DIABs, 35 ± 2.3 vs 25 ± 2.7 mmHg) at reduced LVWI (7.5 vs 10 Kg-m/m²/min.). Similarly, the HR (102 ± 5.2 vs 112 ± 6.9 beats/min.) and mean systemic pressure (115 ± 6.1 vs 120 ± 7.1 mmHg) were lower ($p < .05$) at angina in the DIABs, while exercise work loads were not significantly different.

These preliminary data indicate that equally severe angiographic coronary artery disease is more poorly tolerated by ischemic, diabetic myocardium compared to non-diabetic, suggesting a hemodynamic basis for the clinical deterioration frequently noted in diabetic CHD patients. Furthermore, the reduced pressure-rate product at angina may indicate impaired oxygen delivery at a level more distal to large epicardial vessels visualized by coronary angiography.

CICC 2-05-607

PREVENTION OF ANGINA RELATED LEFT VENTRICULAR FUNCTION BY PERHEXILINE. C.J. Pepine, S.J. Schang and C.R. Bemiller. Naval Hospital, Philadelphia.

Left ventricular (LV) hemodynamic and metabolic dysfunction during myocardial ischemia incident to angina pectoris occurs regularly. The effects of perhexiline, a new, non-nitrate, non- β -blocker anti-anginal agent on these LV responses were studied in 21 angina patients with angiographically documented coronary artery disease.

LV measurements during exercise and atrial pacing, before and after perhexiline, included LV filling pressure (LVFP), stroke work index (SWI), heart rate (HR), systemic pressure (SPm) and myocardial lactate extraction. During exercise, at identical work loads, perhexiline increased SWI (before \rightarrow after perhexiline) ($68 \pm 6 \rightarrow 89 \pm 5$ Gm-m/b/m², $p < .05$) at reduced LVFP ($26.4 \pm 3.0 \rightarrow 18 \pm 2.8$ mmHg, $p < .02$) and HR ($114 \pm 5 \rightarrow 105 \pm 3.4$ b/min., $p < .05$), while angina was either not evoked or delayed in 17 of 20 patients. When the effect of perhexiline on HR was prevented by atrial pacing at similar SPm ($107.7 \rightarrow 107.3$ mmHg), the angina threshold to tachycardia increased in 16 of 20 patients associated with enhanced lactate extraction ($-4.5 \rightarrow +6.8\%$) in 15 patients.

Perhexiline prevents exercise-induced angina and related hemodynamic deterioration while lowering the exercise HR. When HR is controlled, the favorable

action of perhexiline persists with an increase in the angina threshold to tachycardia and decreased myocardial anaerobiosis. These data suggest that perhexiline is a useful medical adjunct for the management of patients with angina pectoris.

CICC 2-05-602

AUGMENTATION OF LIPID REDUCTION ACTION OF D-THYROXINE (DT₄) WITHOUT FACTITIOUS HYPERTHYROIDISM. C.J. Pepine and S.J. Schang. Naval Hospital, Philadelphia.

Although hyperlipidemia (HL) is associated with increased coronary heart disease (CHD), it has not been established whether lowering serum lipids has an effect on the morbidity and mortality due to CHD. The response to current anti-HL therapy is often limited either by decreased effectiveness or side effects. DT₄, a potent anti-HL agent, is of limited use in CHD patients because of reported exacerbation of angina pectoris (AP). To examine the possible benefit of combined therapy with propranolol (P) (to block undesirable oxygen-wasting tachycardia) we treated 28 male patients (mean age 44.5 years) with HL (12 Type II and 16 Type IV) and AP.

After diagnostic catheterization studies each patient's anginal syndrome was controlled with P. Following appropriate dietary restrictions and body weight reduction (mean weight 179.9 ± 5.2 lbs.), serum cholesterol (CHOL) (mean 298.0 ± 12.6 mg%) and triglycerides (TRIG) (261.8 ± 37 mg%) stabilized. After 21.7 months (mean) with DT₄ (mean dose 7.5 mg/day) serum CHOL (255 ± 11.6) and TRIG (221.6 ± 22.2) decreased significantly ($p < .001$), while levels of both lipids normalized in 86% of patients and body weight was unchanged (183.7 ± 6). AP was decreased in 25 and unchanged in three patients. There were no complications or deaths. Five patients have been restudied and coronary angiographic abnormalities, related to persistent HL have progressed in one patient.

While these data are preliminary, it appears that DT₄ can be safely utilized in AP patients when its undesirable effects are blocked with P. Doses > 8 mg/day have been well tolerated by nine patients with extended effectiveness (CHOL -18.4%, TRIG -18.1%) from control determinations.

CICC 3-05-150

MYOCARDIAL DEPRESSION: AN UNDESIRABLE ANTI-ANGINAL EFFECT OF PROPRANOLOL? C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

The success of propranolol (P) in treating angina pectoris (AP) has led to the development of β adrenergic blocking agents with a more favorable ratio of β receptor blocking action to intrinsic myocardial depression. To determine the effect of these agents on AP and left ventricular (LV) function, resting and exercise measurements of LV end-diastolic pressure (LVEDP), the rate at which ventricular pressure increases during contraction (dp/dt), stroke work index (SWI) and heart rate (HR) were made with, and without, practolol (10 mg), KO 1313 (10 mg), and KO 1366 (2.5 mg), and compared to P (10 mg).

Significantly depressed LV function (\downarrow SWI/LVEDP) during exercise was not observed with practolol (SWI/LVEDP -4.8% from control), KO 1313 (+5.9%), or KO 1366 (+2.2%), whereas P markedly \downarrow SWI/LVEDP [-32% ($p < .01$)]. Exercise LV dp/dt declined with practolol (-12.2%), KO 1313 (-19%), and KO 1366 (-18%), related to significant ($p < .05$) reduction of exercise HR (practolol, -11%; KO 1313, -10.8%; KO 1366, -15.6%). P's depression of LV dp/dt (-31%) could not be attributed solely to its modest attenuation (-7.3%) of exercise HR. Practolol increased AP threshold in 6 of 12, KO 1313 — 3 of 12, KO 1366 — 1 of 6, but P was effective in 14 of 16 patients.

In conclusion, intrinsic LV depression induced by P appears to be a major factor associated with its more favorable anti-anginal effect when compared to potent blocking agents with less cardiac depression.

CICC 2-05-612

USE OF DIGITALIS AND PROPRANOLOL. C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

Heart failure often limits the usefulness of beta-blocking agents especially in patients with arrhythmia or angina. Since digitalis inotropism is independent of adrenergic activity, the effect of incremental doses of acetylstrophanthidin (AS) alone, and after propranolol (P), was studied in 24 intact dogs.

Left ventricular pressures, the rate at which ventricular pressure increases during contraction (dp/dt), and aortic flow velocity (AVF) were recorded before and after AS 0.025 mg/kg, a digitalizing dose. P (0.5 mg/kg) was infused in 12 dogs following initial AS dose. Then, all dogs received additional AS (0.025 mg/kg) at 15-minute intervals. Heart rate was maintained (atrial pacing) at pre-AS rate and measurements were made until ventricular tachycardia (VT) supervened. The initial AS dose increased V max (dp/dt/K [P-LVEDP]

extrapolated to 0) $1.91 \pm 0.18 \rightarrow 3.02 \pm .34$ ml/sec. and AVF $78 \pm 10 \rightarrow 102 \pm 16$ cc/sec. Subsequent AS increased V max (3.62 ± 138) until VT at $0.078 \pm .011$ mg/kg AS. P initially reduced V max ($3.98 \pm .42$) and AVF (110 ± 18), prior to VT. Accordingly, P delayed VT and permitted a larger cumulative AS dose (0.106 ± 0.18 mg/kg) $p < .05$.

These data indicate that P-induced myocardial depression is significantly ($p < .01$) reversed by the independent positive inotropism of cumulative doses of AS as VT is suppressed. Consequently, in clinical conditions where beta-blockade is desirable, P may be used despite the presence of heart failure if additional glycoside is administered.

CICC 3-05-153

LATENT OR ASYMPTOMATIC PHASE OF CORONARY HEART DISEASE (CHD). C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

Since most CHD patients who die suddenly are asymptomatic, identification of patients with latent CHD is necessary. A study was undertaken to characterize clinical features, coronary anatomy, electrocardiogram (ECG), hemodynamics, and myocardial metabolic responses of young, asymptomatic patients with a family history of CHD and hyperlipemia. Xanthomas were present in 23.8%, obesity in 33%, hypertension in 42.8%, and abnormal glucose tolerance test (GTT) in 52.4%, while only 18% had abnormal exercise ECGs.

Pacing and exercise LV function was normal despite evidence of ischemia (S-T segment or abnormal lactate extraction) in 43%. Coronary arteriography demonstrated significant coronary artery disease (CAD), $> 50\%$ obstruction in 57%. No correlation was evident between the presence and extent of CAD and other clinical features in these high-risk asymptomatic patients.

Significant myocardial ischemia and CAD exist in the absence of symptoms. Furthermore, current screening techniques are poor discriminators of advanced asymptomatic CHD in high-risk patients.

A definitive major publication of this work is in progress.

MR041.20.01-0363

RELATIONSHIP OF ANGINAL SYMPTOMS TO LUNG MECHANICS DURING MYOCARDIAL ISCHEMIA. C.J. Pepine and L. Wiener. Naval Hospital, Philadelphia.

The angina pectoris syndrome (AP) typically includes sensations of chest tightness or difficulty in

breathing. Left ventricular (LV) dysfunction during myocardial ischemia incident to AP is now well documented. Since secondary alterations in lung mechanics could relate to these symptoms, we examined airway resistance (Raw), lung volume (TGV), lung compliance (C_L) and LV pressure-volume relations during pacing-induced AP.

LV end-diastolic pressure (EDP) increased suddenly with AP (mean +41%, $p < .01$), without change in end-diastolic volume (EDV). LV distensibility (EDV/EDP) decreased abruptly (-37%, $p < .01$), with reduction in airway conductance ($1/\text{Raw}/\text{TGV}$) -40%, $p < .05$, and C_L declined (-27%, $p < .05$). When AP was relieved by cessation of pacing, these changes returned toward pre-angina levels.

Ischemia-induced LV dysfunction abruptly increases LVEDP. The resulting increased pulmonary capillary pressure effects an alteration of lung mechanics consisting of increased Raw and reduced C_L . The changes in ventilatory effort which ensue may be interpreted by the AP patient as chest tightness, heaviness, or constriction.

MR041.20.01-0133

CORONARY HEMODYNAMIC AND METABOLIC EFFECTS OF PROPRANOLOL (P) AND NITROGLYCERIN (NTG) IN ISCHEMIC HEART DISEASE. S.J. Schang and C.J. Pepine. Naval Hospital, Philadelphia.

The anti-anginal action of P and NTG has been largely attributed to net reduction of mechanical determinants of left ventricular (LV) oxygen consumption ($\text{LV}\dot{\text{V}}\text{O}_2$). Whether these effects are adequate to prevent a shift to anaerobic metabolic pathways in patients with ischemic heart disease has not been determined. We therefore measured coronary sinus blood flow (CSBF) by continuous thermodilution, $\text{LV}\dot{\text{V}}\text{O}_2$, LV lactate consumption ($\text{LV}\dot{\text{V}}\text{L}$), cardiac index (CI), and systemic pressure (SPm) in 14 patients (mean age 47.7 years) with stable angina pectoris (AP). Determinations were made at rest with heart rate (HR) controlled by pacing, and during AP evoked by atrial tachycardia (T), before and after P (10 mg intravenously), and P+NTG (0.3 mg sublingually).

Resting $\text{LV}\dot{\text{V}}\text{O}_2$ did not change after P ($12.8 \pm .86 \rightarrow 12.1 \pm 1.0$ cc/min), at the same HR, while $\text{LV}\dot{\text{V}}\text{L}$ decreased in 10 patients. During T, at identical HR, $\text{LV}\dot{\text{V}}\text{O}_2$ before \rightarrow after P increased similarly ($17.1 \pm 1.4 \rightarrow 16.8 \pm 1.6$ cc/min) as tension time index (TTI) increased ($2968 \pm 132 \rightarrow 3017 \pm 115$ mmHg-sec). Increased $\text{LV}\dot{\text{V}}\text{L}$ occurred in nine patients, while AP was lessened or not evoked in eight patients. LV efficiency

($\text{LV eff} = \text{LV work index}/\text{LV}\dot{\text{V}}\text{O}_2$) decreased 20% ($p < .01$) compared to control. The addition of NTG at same resting HR reduced $\text{LV}\dot{\text{V}}\text{O}_2$ (-9%, $p < .05$), as myocardial oxygen requirements decreased TTI (-11%, $p < .05$). During T, $\text{LV}\dot{\text{V}}\text{O}_2$ increased less ($16.8 \pm 1.6 \rightarrow 13.9 \pm 1.1$, $p < .05$) than after P, as AP lessened or did not occur in 9 of 14 patients and $\text{LV}\dot{\text{V}}\text{L}$ was unchanged.

These data indicate that the anti-anginal effect of P persists when HR is controlled. Both P and P+NTG have beneficial effects on myocardial oxygen delivery, preventing metabolic deterioration.

CICC 3-05-148

TREADMILL EXERCISE TEST PERFORMANCE IN A GROUP OF PATIENTS SIX MONTHS POST-MYOCARDIAL INFARCTION: CORRELATION WITH DIAGNOSTIC CORONARY ARTERIOGRAPHY. C.W. Shaeffer; S.C. Smith, Jr.; R.G. Daly; and P. Goldfinger. Naval Hospital, Portsmouth, Va.

A total of 23 patients who are 8- to 10-months post acute myocardial infarction have undergone submaximal treadmill exercise testing by the method of Bruce, et al. There has been a high incidence of negative treadmill tests approximating 65% in these patients. The great majority have attained heart rates greater than 90% of their maximal anticipated rates. There has not been a correlation between symptoms and treadmill-test positivity.

The test has been useful in situations where extreme positivity was a consideration in the selection of patients for contemplated coronary artery surgery. Additionally, the test has provided aid in counseling active duty career naval personnel regarding future duty and civilian employability.

CICC 2-08-505

A REVIEW OF CORONARY CARE UNIT EXPERIENCE AT A LARGE MILITARY TEACHING HOSPITAL, 1967-1971. C.W. Shaeffer; S.C. Smith, Jr.; and P. Goldfinger. Naval Hospital, Portsmouth, Va.

The review of a 4-year experience of the Portsmouth Naval Hospital Coronary Care Unit has begun. Approximately 200 records have been reviewed, and of the total number of admissions to the Coronary Care Unit, only 50%, approximately, have been found to have a diagnosis of acute myocardial infarction. Additionally, the mean age of the patients with myocardial infarction, which was initially presumed to be quite low, has been found to approximate 56 years, somewhat older than originally anticipated.

Review of the unit's experience is continuing. Further reports will detail mortality and other clinical characteristics which may make this unit unique in the type of population served.
CICC 2-08-512

COMPARISON OF FOUR DIGOXIN PREPARATIONS PRODUCED BY A SINGLE MANUFACTURER. W. Vieweg, J. Sode, L. Kilmer and S. Fidler. Naval Hospital, Bethesda.

Reported variations in biologic availability of digoxin tablets prompted us to evaluate digoxin preparations obtained from our hospital pharmacy. All were manufactured by the Burroughs Wellcome Company. Each of four healthy volunteers was studied four times (at 1-week intervals) in an identical manner, except that 0.5 mg of a different digoxin preparation was given each time. Blood was obtained at 0, ½, 1, 1½, 2, 3, and 5 hours after drug administration. Lots A, B and C consisted of digoxin tablets. Lot D was digoxin elixir (.05 mg/ml). Serum digoxin was measured by radioimmunoassay. Mean +SD peak values (ng/ml) were:

Lot A 1.42 + 0.20	Lot C 1.22 + 0.11
Lot B 1.68 + 0.54	Lot D 2.96 + 1.10

Mean peak serum digoxin values, as well as mean values at each point on the absorption curve, were not statistically different for the three tablets tested; and the 5-hour values were essentially the same at 0.5 ng/ml. Digoxin elixir yielded a higher peak in 30- and 60-min. serum digoxin concentrations ($p < .05$) than two of the tablet preparations. However, after 90 min., serum digoxin levels obtained following elixir and tablets were again comparable. Thus the three lots of digoxin tablets tested showed acceptable and comparable biologic availability. Because of more rapid early absorption and possible greater total absorption, digoxin elixir and tablets should be used interchangeably with caution.
CICC 2-06-313

THE EFFECT OF DIGOXIN (DIG) ON SALIVARY ELECTROLYTES IN MAN. W. Vieweg, J. Sode, S. Fidler, L. Kilmer and D. Lee. Naval Hospital, Bethesda.

A recent report that the salivary Ca and K concentration product (Ca x K) yields important information concerning the presence of digitalis toxicity in man prompted us to measure serum and salivary DIG as well as salivary K, Ca, and Na in four healthy males, before,

and serially after, the oral administration of 0.5 mg. of DIG. Each subject was studied on three different occasions. The studies were performed at intervals of one week, or more. Whole saliva was collected and centrifuged prior to analysis. DIG was measured by radioimmunoassay; Na and K by flame photometry; and Ca by ethylenediamine tetraacetic acid (EDTA) titration. Mean values were:

Time(hours)	0	1	2	3	5
Serum DIG(ng/ml)	0.0	1.25	0.97	0.71	0.50
Salivary DIG(ng/ml)	0.0	0.62	0.61	0.40	0.27
Salivary K(mEq/L)	22.3	24.1	24.4	23.7	25.8
Salivary Ca(mEq/L)	2.9	2.8	3.2	3.4	3.8
Salivary Na(mEq/L)	12.3	9.83	9.25	9.25	10.9
Salivary Ca x K	65	66	72	83	105

The mean salivary/serum DIG concentration ratios at ½, 1, 1½, 2, 3, and 5 hrs. after the dose were 0.5, 0.5, 0.56, 0.63, 0.56, and 0.54, respectively. After DIG, mean salivary K and Ca rose, while salivary Na declined. Mean salivary K, Ca, and Ca x K, 5 hours after the dose, were significantly higher than base line ($p < .05$). The data show alterations in salivary electrolytes following low doses of DIG and suggest a DIG effect on the salivary electrolyte transport.
CICC 2-06-313

METABOLIC CHANGES DURING EXERCISE IN PATIENTS WITH KNOWN ISCHEMIC HEART DISEASE. W.V.R. Vieweg, J. Sode, L.M. Fox and S.M. Fidler. Naval Hospital, Bethesda.

The results of preliminary observations raise the possibility that, in patients with coronary artery disease, the fasting FFA/βOHB (Free Fatty Acid to Beta Hydroxybutyrate ratio) may serve to detect a tendency for preferential esterification of metabolic substrates to form triglycerides. These patients may show an accentuated catecholamine and lipolytic response to exercise.
CICC 2-06-324

2,3, DIPHOSPHOGLYCERATE LEVELS AND OXY-HEMOGLOBIN DISSOCIATION IN PATIENTS WITH ISCHEMIC HEART DISEASE AND ATYPICAL CHEST PAIN. J.W. Weaver, A.D. Hagan and J.E. Lang. Naval Hospital, San Diego.

The purpose of this study will be to reproduce and standardize abnormalities in 2,3 diphosphoglycerate levels and oxyhemoglobin dissociation curves, in

patients with known coronary artery disease. The same determinations will be performed on patients with atypical chest pain to determine if any abnormality exists which could be used to distinguish between those with, and those without, coronary artery disease. Control patients will be selected from those patients who have clinical angina pectoris and have angiographically proved coronary artery disease. Oxyhemoglobin dissociation (P_{50}), and 2,3 diphosphoglycerate levels will be obtained both when asymptomatic and during an attack of angina pectoris induced by exercise. Other patients will be selected because of complaints of chest pain which is atypical. They will undergo similar laboratory studies under similar conditions. Finally, coronary angiography will be performed on the patient with atypical chest pain to verify or deny the presence of coronary artery disease.

To date, progress has consisted of a literature search for background and related information, and development of an outline of the protocol to be followed for studying the control and experimental patients. Patients with atypical chest pain are being selected from the Cardiology Clinic for study, as well as known coronary artery disease patients who will serve as controls. CICC 3-16-041

RADIOISOTOPIC DETERMINATION OF GLOMERULAR FILTRATION RATE (GFR) AND EFFECTIVE RENAL PLASMA FLOW (ERPF). G. John Weir, Jr. Naval Hospital, Great Lakes.

Determination of ERPF has not become a common clinical aid because of the difficulty of chemical determinations of para-aminohippuric acid. Clinical GFR determinations are approximated by using creatinine clearance because of similar problems with inulin. This necessitates 24-hour urine collections, an error-prone procedure.

A technique has been developed which permits determination of ERPF and GFR, alone or simultaneously, from the plasma disappearance curves of radioactive compounds. No urine collections are necessary. A single injection of the radioactive compound is utilized. Determinations require approximately two hours of patient time and six blood samples drawn at specified times, following injection.

Using this technique 25 measurements were made on 17 normal people. ERPF was 561 ± 115 ml/min (mean \pm standard deviations); GFR was 190 ± 47 ml/min (both values corrected to 1.73 m^2 body surface area).

Recently 99m-Tc labeled DTPA (diethylenetriamine-pentacetic acid) has been used for GFR measurements.

The high photon flux of this nuclide reduces statistical variations and radiation exposure to the patient. CICC 2-13-009

DERMATOLOGY

APPLICATION OF THE NITROBLUE TETRAZOLIUM DYE TEST TO SELECTED DERMATOLOGIC DISORDERS. H.B. Allen. Naval Hospital, Philadelphia.

The nitroblue tetrazolium (NBT) dye test which has previously been shown to be an important laboratory aid in diagnosing bacterial infections has been evaluated in patients with dermatologic diseases. This study of 75 patients has shown a positive response (greater than six dye-containing cells per 100 neutrophils) in all bacterial diseases tested. Viral and fungal disorders have yielded negative results. Fourteen patients with urticaria have been studied; nine had negative tests; four of the five remaining had positive NBT tests which subsequently became negative after antibiotic therapy. The application of this test to other dermatologic disorders, which may have a bacterial etiology is proposed.

CICC 3-05-172

DERMATOSIS PAPULOSA NIGRA: AN ELECTRON MICROSCOPIC STUDY. J.G. Beidler, R.C. Charles, and B.L. Johnson. Naval Hospital, Philadelphia.

An unusual case of dermatosis papulosa nigra in a 15-year-old black girl is currently under study. Electron microscopic sections have been obtained and preliminary investigation indicates excessive production of immature collagen fibrils, by fibroblasts located in the papillary dermis. Further evaluation of these features is in progress.

CICC 2-05-621

ETIOLOGY OF HYPOPIGMENTATION IN TINEA VERSICOLOR INFECTIONS UTILIZING HISTOCHEMICAL AND ELECTRON MICROSCOPIC METHODS. R.C. Charles, B.L. Johnson and J.G. Beidler. Naval Hospital, Philadelphia.

Hypopigmentation in tinea versicolor has been studied and the results have been submitted. The second phase of this study is to study the mechanisms of hyperpigmentation, utilizing the methods of epidermal turnover, dihydroxyphenylalanine (DOPA)-stained

epidermal whole mounts and electron microscopy of hyperpigmented affected lesions and adjacent normal controls. Four patients are planned for inclusion in this phase of the study.
CICC 2-05-619

ANTIBODY RESPONSE TO TRIBROMOSALICYLANILIDE-PROTEIN COMPLEX. J.H. Dunne and H.L. Parlette. Naval Hospital, Philadelphia.

The mechanism of photoallergic contact dermatitis associated with the halogenated salicylanilides is unknown. The two most widely accepted hypotheses suggest that ultraviolet light acts directly on the unbound salicylanilide, either by forming a free radical which is attached to epidermal protein to form a hapten-protein complex, or by degrading the salicylanilide into a different compound which acts as a simple contact allergen independent of light.

This study will examine the effects of long-wave ultraviolet light (320-400 nm) on 3, 4, 5 tribromosalicylanilide-protein complexes which were formed in the dark. The antigenic specificity of unirradiated and irradiated 3, 4, 5 tribromosalicylanilide protein will be studied by comparing specific antihapten antibody by Ouchterlony gel diffusion and passive cutaneous anaphylaxis.

Since this is a recently funded project little progress can be reported at this time. Current efforts are directed toward selecting a carrier protein and characterizing the unirradiated and irradiated complexes by spectrophotometry and disc-gel electrophoresis.
CICC 3-05-196

THE USE OF ENZYME-LABELED ANTIBODIES FOR THE LOCALIZATION OF TISSUE ANTIBODIES. G.T. Izuno and J.B. Bridenstine. Naval Hospital, San Diego.

This peroxidase study was undertaken as a means of evaluating skin lesions for the presence of specific immunoglobulins such as are characteristically found in diseases such as lupus erythematosus, pemphigus vulgaris and bullous pemphigoid. We initially experienced difficulty in processing frozen tissue, especially in properly aligning and orienting very small pieces of mouse kidney or smaller fragments of human skin but these factors have been controlled during the last two months.

We are now able to easily determine positive tests but, at present, our main problem has been the inability to accomplish sufficient peroxidase labeling of antibody so as to effectively differentiate specific patterns

of ANA (antinuclear antibody) reactions. We are currently working with and evaluating methods such as: using larger volumes of labeled antibodies, adding 0.25 molar sucrose, and using counterstains such as methylene blue in an effort to overcome this problem. We have done some direct immunofluorescence and peroxidase labeling work on skin specimens, but the numbers are few and we will not have reproducible results unless we overcome our technical problems with the indirect ANA tests. Ultimately, we anticipate applying the techniques used in this study not only to the study of immune skin diseases, but also to the evaluation of the clinical lesions and antisera of patients with primary syphilis.
CICC 3-16-034

ERYTHROPOIETIC PROTOPORPHYRIA: AN ELECTRON MICROSCOPIC STUDY. B.L. Johnson, J.G. Beidler and R.C. Charles. Naval Hospital, Philadelphia.

Electron-microscopic investigation of the involved dermis and epidermis of two male patients with erythropoietic protoporphyria demonstrated peri-fibroblastic abnormal material, indistinctness of the fibroblastic plasma membranes, dilated cisternae within fibroblasts containing this material, desmosome-like and half-desmosome-like dense plaques between opposed fibroblastic surfaces, and impingement of this same substance upon the basement lamina beneath the epidermis. These findings substantiate an active role for the fibroblast in the production of the abnormal hyaline-like material in this disease and are in agreement with recent electron-microscopic studies on lichen amyloidosis, colloid milium, and lipid proteinosis.

New additional findings were the presence of electron dense bodies resembling ingested erythrocytes in numerous dermal fibroblasts and paramyxovirus-like particles within the endoplasmic reticulum of these and other fibroblasts. It appears that erythropoietic protoporphyria shares with the above diseases the characteristics of metabolically abnormal fibroblasts.
CICC 2-05-620

CHARACTERIZATION OF THE INVERTED FOLLICULAR KERATOSIS: A CLINICOPATHOLOGIC CORRELATION. B.L. Johnson, W.A. Schrader and J.F. Russo. Naval Hospital, Philadelphia.

Thirty cases of inverted follicular keratosis have been studied, and are presently being analyzed in terms of the histological characteristics, host reaction, site of origin, and presence of ground subcutaneous changes.

All these histological features are being correlated with the clinical course, site, distribution, and therapy.
CICC 3-05-149

ENDOCRINOLOGY — METABOLISM

CALIBRATION OF WHOLE BODY COUNTERS (WBC) TO DETERMINE TOTAL BODY POTASSIUM (TBK) IN HUMAN SUBJECTS OVER A WIDE RANGE OF BODY WEIGHT. W.M. Beckner and J. Sode. Naval Hospital, Bethesda.

Whole body gamma ray spectrometry is a valuable clinical tool for detecting serial changes in body composition and K balance in individual subjects. Determinations of TBK by WBC, however, require calibration of the system. A WBC may be used to determine a subject's (SUBJ) TBK if the relative counting efficiency (geometry factor) of detecting the gamma rays from ^{40}K in the SUBJ TBK, in relation to ^{40}K in a K standard (STD), has been determined for the subject's size.

Twenty-two (22) subjects, 46 to 167 Kg body weight, were administered 1-2 uCi (curie = standard measure of activity) $^{42}\text{K}_2\text{CO}_3$ to determine a geometry factor (G) for their respective body weights. Since body distribution and gamma-ray energies of ^{42}K and ^{40}K are essentially the same (1.53 and 1.46 mev), the G for ^{40}K may be assumed to be the same as that determined for ^{42}K . For these observations the determined G, as a function of SUBJ body weight, is $0.00265 \text{ Kg} + 0.07$ for WBC number 1 and $0.00272 \text{ Kg} + 1.21$ for WBC number 2. A patient's TBK may now be determined from only his ^{40}K according to the following equation:

$$\text{Gms. K(SUBJ)} = \frac{{}^{40}\text{K(SUBJ)}}{{}^{40}\text{K(STD)}} \times \text{G} \times \text{Gms. K(STD)}$$

Calibration of the WBC over this wide range of body weight will make single TBK determinations clinically more meaningful.

CICC 2-06-323

DEPRESSION OF THE STIMULATION OF ETHANOL OXIDATION BY FRUCTOSE OR PYRUVATE IN LIVER CELLS FROM HYPERTHYROID ANIMALS. M.N. Berry and H.V. Werner. Naval Hospital, Oakland.

The basal rate of ethanol oxidation was the same in cells from normal and hyperthyroid animals. But, ethanol oxidation was stimulated only 66% in cells from

thyroxine-treated rats compared with a stimulation of 185% in cells from control animals. Associated with this depression of fructose-stimulated ethanol oxidation in the hyperthyroid state was a marked decrease in the accumulation of reduced products of fructose metabolism, namely, sorbitol, glycerol, and glycerol-1-phosphate. Fructose and its metabolites promote ethanol oxidation by acting as cytoplasmic hydrogen acceptors and by providing carrier molecules for the operation of the glycerol-phosphate shuttle. In the hyperthyroid state the mitochondrial limb of the glycerol-phosphate shuttle is greatly stimulated, but the cytoplasmic coupled reactions of ethanol, with fructose and its metabolites are markedly depressed. In consequence reduced products of fructose metabolism do not accumulate and the entry of ethanol hydrogen into the mitochondria by way of the glycerol-phosphate shuttle is impaired. In the hyperthyroid state the stimulation of hepatic ethanol oxidation by pyruvate is depressed and there is a corresponding diminution in the rate of lactate accumulation. This implies that the cytoplasmic redox reaction between pyruvate and ethanol, mediated by lactate dehydrogenase and alcohol dehydrogenase, takes place less readily in cells from hyperthyroid animals. In view of these findings the results of studies of the effects of thyroxine on the "redox state" of the cytoplasmic compartment of the hepatic cell may require reevaluation.

MR041.20.01-0383

MEASUREMENT OF PRODUCTION RATES AND METABOLIC CLEARANCE RATES OF GROWTH HORMONE AND CORTISOL IN STRESS SITUATIONS IN NAVAL PERSONNEL. P. Cianci and R.L. Weinstein, Naval Hospital, Oakland; **R.E. Reitz and H.V. Werner.** University of California, San Francisco.

In certain stress situations, such as fasting, there is glucose intolerance. The mechanism for glucose intolerance in fasting has not been explained. Some investigators assume that the carbohydrate intolerance is due to elevation in circulating free fatty acids. However, the relative contribution of growth hormone and cortisol, both of which are diabetogenic hormones, has not been determined. By studying the circulating plasma levels and the total amount of each hormone produced during such stress situations, the relative importance of these two hormones can be determined. Radioactive growth hormone or cortisol, highly purified and sterile, has been administered intravenously to subjects, both in the fed and fasting state; subsequent determinations of metabolic clearance rates and production rates have been based on these infusion studies.

In the stress of fasting it has been demonstrated that the metabolic clearance rates of growth hormone decrease, while the peripheral plasma concentration increases. There is a marked increase in production of growth hormone in the pituitary and this is more pronounced when nicotinic acid is given to depress the elevated concentrations of fatty acids. These studies suggest that a feedback mechanism exists between levels of fatty acids and the release of growth hormone in the fasted state, and that the elevation of growth hormone, which was observed during nicotinic acid suppression of fatty acids, is explained on an increased-production basis (vice decreased metabolic clearance). The fact that no rise in plasma cortisol was observed, when growth hormone concentrations increased, implies that this is not explained simply as a stress response to the nicotinic acid.

MR041.20-01-0340

THE EFFECT OF DIPHENYLHYDANTOIN (DILANTIN) ON THE KINETICS OF GLUCOSE METABOLISM AND INSULIN SECRETION IN VIVO. G.E. Gorsuch. Naval Hospital, Oakland.

A number of pharmacologic agents (e.g., mannoheptulose, glucosamine, 2-deoxy-d-glucose, dinitrophenol, cyanide, etc.) have been shown to inhibit glucose-induced insulin release, presumably by inhibition of certain enzymatic steps along the pathway of glucose metabolism. Similarly, diphenylhydantoin has been shown to completely inhibit the immunoreactive insulin response to glucose in the isolated perfused pancreas, apparently by accelerating the sodium-pump mechanism to reduce essential intracellular sodium concentration and calcium uptake.

During the past two years application of these findings has been extended to the study of the effect of diphenylhydantoin on glucose metabolism and insulin secretion in the human milieu in association with the Metabolic Research Unit, University of California, San Francisco. The basic experimental design consists of a five-hour oral glucose tolerance test and an intravenous glucose tolerance and arginine stimulation test performed before, and after, diphenylhydantoin therapy.

CICC 3-48-213

PLASMA TESTOSTERONE (T) AS AN INDEX OF GONADOTROPIN SECRETION IN PATIENTS WITH PITUITARY TUMORS. R. Johnsonbaugh, J. Kleiman, S. Fidler, J. Sode and M. Cohen. Naval Hospital, Bethesda.

Low values of urinary and plasma gonadotropins in males are uncertain indices of diminished gonadotropin secretion unless associated with testicular atrophy. In order to better evaluate the significance of low gonadotropins in patients with pituitary tumors during the reproductive age, a radioimmunoassay for T was developed utilizing an antibody supplied by Loriaux and Lipsett of the Nat. Inst. of Health. The assay involves ether extraction of 1 ml of plasma and separation of testosterone from other steroids by thin layer chromatography. An 18-hour incubation time is required. The tracer used is 3H-testosterone.

The normal range for T by this method was 0.3-1.0 ng/ml for females and 3-10 ng/ml for males. T levels in four male patients aged 25 to 42 years, with eosinophilic pituitary tumors, were 1.6, 2.4, 4.3, and 15 ng/ml, and; in four females aged 16 to 45 years, with eosinophilic pituitary tumors, the levels were 0.2, 0.4, 0.5 and 0.2 ng/ml. One male with a very low T value (0.5 ng/ml) had markedly decreased libido. In males, the association of low T with hypogonadotropinuria was a useful parameter in following the natural history of pituitary tumors. Simultaneous measurements of these hormones should also be helpful in evaluating the efficacy of various therapeutic modalities.

CICC 3-06-131

ESTRADIOL AND TESTOSTERONE SECRETION BY HUMAN, SIMIAN, AND CANINE TESTES, IN MALES WITH HYPOGONADISM AND IN MALE PSEUDO-HERMAPHRODITES WITH THE FEMINIZING TESTES SYNDROME. R.P. Kelch, M.R. Jenner, R. Weinstein, S.L. Kaplan and M.M. Grumbach. Naval Hospital, Oakland.

The role of the human testis in the production of 17 α -estradiol (E₂) was investigated by determining the concentration of E₂ and testosterone in peripheral and spermatic vein plasma samples. Specimens were obtained from eight normal men, three men with hypogonadism, and two patients with the incomplete form of the feminizing testes syndrome. For comparison, similar studies were performed in four monkeys, 10 mongrel dogs, and four additional dogs who were given 1000 IU of human chorionic gonadotropin (HCG)/day for five days. Plasma E₂ was measured by radioimmunoassay utilizing sheep anti-E₂ serum. In the eight normal men, the mean peripheral vein E₂ concentration

was 20 ± 1.6 pg/ml, while the spermatic vein concentration was 50 times as great, 1049 ± 57 pg/ml. All three patients with testicular abnormalities had low spermatic vein E_2 concentrations (160, 280 and 416 pg/ml). Lesser E_2 gradients were found across the simian (threefold) and canine (approximately 12-fold) testes. Testicular testosterone gradients (human 110-fold, simian 10-, and canine 77-fold) were greater than the E_2 gradients in all three species. In four dogs, HCG treatment elicited a sixfold increase in peripheral and a ninefold increase in spermatic vein testosterone concentrations; however, peripheral and spermatic vein E_2 concentrations did not differ from control values. Spermatic vein E_2 concentrations were > 4600 and 2210 pg/ml (post-HCG) in two patients with the incomplete form of the feminizing testes syndrome. CICC 3-48-121

DISCORDANT SERUM GROWTH HORMONE (GH) RESPONSES TO IV AND IM ADMINISTRATION OF SYNTHETIC 1-24 CORTICOTROPIN (ACTH). B.S. Keenan, R.E. Johnsonbaugh and J. Sode. Naval Hospital, Bethesda.

Large IV (intravenous) doses (0.5-1.0 mg) of 1-24 ACTH acutely stimulate GH secretion in man. Such doses are 2-4 times higher than the dose required (0.25 mg) for maximal steroidogenesis, and it is not currently known whether this effect of 1-24 ACTH is nonspecific or pharmacologic in nature, or whether ACTH has a regulatory role in GH secretion. For this reason we measured immunoreactive GH and fluorometric serum cortisol in 17 euendocrine patients after IV ($n = 10$) and IM (intramuscular) ($n = 7$) administration of 0.25 mg of 1-24 ACTH. Blood was obtained from most patients by multiple venipunctures.

The serum cortisol responses were similar in both groups (mean peak value 42.5 mcg% after IV and 38.3 mcg% after IM). The GH responses, however, were markedly discordant. In the IV group, seven of the 10 subjects tested responded with significant increments in GH within 15-30 min. (mean peak value 29.1 ng/nl), whereas, only one of the seven subjects given IM 1-24 ACTH had an acute rise in GH.

The data show that steroidogenic and GH responses to 1-24 ACTH can be discordant, and suggest a dose-dependent pharmacologic effect of ACTH on GH secretion rather than a regulatory relationship between these two hormones. The IM administration of 0.25 mg 1-24 ACTH produces near-maximal steroidogenic response but is of no use in the diagnostic evaluation of GH deficiency.

MR041.06.01-0028

SPECIFIC METABOLIC EFFECTS OF VARIOUS TYPES OF INJURY TO THE LIVER. V.H. Fitchett, R.M. Deaner and D.E. Hutchison. Naval Hospital, Oakland.

After trauma, the extent of liver recovery may be judged by functional ability to accomplish certain anabolic tasks, e.g., gluconeogenesis (formation of glucose from lactate). Following a control lactate tolerance test (LTT), 2 mEq/kg, liver blood supply was interrupted and the organ thoroughly flushed with iced saline (750 ml at 4°C) for 15 minutes. A second LTT was performed, with simultaneous blood samples drawn from the portal and hepatic veins for assay of glucose, lactate and pyruvate. Liver biopsy samples for glycogen content were also obtained at the beginning and end of each test period. The bulk of effort in the completion of this phase of evaluation of ischemic injury on lactic-acid metabolism of dog liver has focused on the influence of blood flow on the determinations.

Ten dogs were studied and evaluated using the flow meter to establish hepatic artery, portal vein, mesenteric vein and hepatic vein flows under various different circumstances in the present model. It has been determined that such factors as laparotomy, anesthesia and paralysis with gallamine triethiodide (Flaxedil), and the performance and closure of a portacaval shunt, have very little influence on the major blood flow to-and-from dog liver. These are factors that could conceivably influence the hepatic cellular activity involved in the perfusion experimental model.

MR041.20.01-4001

CLINICAL EFFECTS OF BETA BLOCKADE ON THYROTOXICOSIS. T.J. Lapine. Naval Hospital Boston, Chelsea, Mass.

The use of beta blockade to suppress the overt clinical effects of thyrotoxicosis has been advocated by some authorities. So far, we have used the drug propranolol (Inderal) in varying doses in an attempt to control symptoms in ten patients.

Improvement has been noted in varying degrees in most patients, in blood pressure, pulse, reflexes, tumor, perspiration and bowel movement. There has been only minimal change in degree of subjective symptoms, i.e., nervousness and mental aberrations. No changes have been noted in thyroid size and severity of exophthalmos.

CICC 3-02-066

HUMAN PARATHYROID HORMONE (HPTH)-CALCIUM (Ca) INTERRELATIONS IN PREGNANCY (P) AND NEWBORN INFANTS. R.E. Reitz, T.A. Daane, J.D. Woods and R.L. Weinstein. Naval Hospital, Oakland, and Department of Medicine, University of California, San Francisco.

The ability to directly measure HPTH (by radioimmunoassay) and ionized serum calcium (Ca^{++}) is of fundamental importance in evaluation of Ca metabolism in P and the newborn. Blood for HPTH, Ca^{++} , and total calcium (TCa) was collected throughout P in 17 subjects in each of the following groups: PI = 8-13 wks, PII = 14-19 wks, PIII = 20-27 wks, and PIV = 28-40 wks. These values were compared to those obtained from eight normal women (N). In addition, blood was obtained from 18 mothers and newborns (cord) at delivery. Mean (\pm S.D.) TCa in PI ($9.44 \pm .42$ mg%) was similar to N ($9.40 \pm .34$ mg%). However, HPTH in PI (544 ± 218 pg/ml) was increased compared to N (289 ± 161 pg/ml) ($p < .01$). Throughout P (I-IV), TCa ($9.44 \pm .42$, $9.28 \pm .32$, $9.33 \pm .38$, $9.37 \pm .48$ mg%) and Ca^{++} ($.94 \pm .05$, $.99 \pm .06$, $1.00 \pm .05$ mM/L) did not change ($p =$ not specified [NS]). HPTH concentrations in PI through PIII (544 ± 218 , 568 ± 165 , 450 ± 191 pg/ml) were similar ($p =$ NS); however, HPTH increased in PIII to PIV (450 ± 191 , 692 ± 250 pg/ml) ($p < .01$). At delivery Ca^{++} ($1.17 \pm .11$ mM/L) and TCa ($11.03 \pm .49$ mg%) in cord blood were increased compared to mother's Ca^{++} ($.96 \pm .04$ mM/L) and TCa ($9.26 \pm .41$ mg%) ($p < .01$); whereas, HPTH (121 ± 108 pg/ml) was decreased compared to the mother's (615 ± 313 pg/ml) ($p < .01$).

Conclusions: (1) HPTH increases early in pregnancy, and further in the third trimester (PIV), when infant skeletal mineralization is greatest. (2) Newborn infants have hypercalcemia and decreased HPTH concentrations compared to mother's at delivery.

CICC 3-48-091

CALCIUM-PARATHYROID HORMONE INTERRELATIONSHIPS IN NORMAL VOLUNTEERS AS A BASIS FOR INTERPRETATION OF VALUES IN INJURIES AND DISEASE IN NAVAL PERSONNEL. R.E. Reitz, University of California, San Francisco (UCSF), and R.L. Weinstein. Naval Hospital, Oakland.

Significant data have been obtained concerning calcium-parathyroid hormone (PTH) relationships in normal adults. Blood levels of these two parameters, collected at different times during the day, have provided us with an acceptable range in normal personnel. Further, we have accurately defined the basal levels of PTH concentration. Several patients with disorders of

parathyroid function have been diagnosed on the basis of these data obtained in normals. In addition to calcium and PTH, magnesium and ionized calcium concentrations have been determined in a number of subjects.

MR041.20.01-0341

ETIOLOGY OF HYPERCALCEMIA IN THYROTOXICOSIS. R.E. Reitz, UCSF, and R.L. Weinstein. Naval Hospital, Oakland.

A significant number of active duty Naval personnel and their dependents develop hyperthyroidism. Many of these patients also manifest hypercalcemia. The hypercalcemia may be related to the increased bone turnover associated with the hyperthyroid state, or it may be due to existing hyperparathyroidism. Not uncommonly this issue is resolved only by surgical exploration.

Several patients with hyperthyroidism have been evaluated and have demonstrated hypercalcemia during the period of hyperthyroidism. These patients have been admitted to the metabolic research ward for detailed studies of calcium metabolism. Samples are being analyzed for total and ionized calcium, magnesium, phosphorus, and parathyroid hormone, during the period of hyperthyroidism and after the hyperthyroid state has remitted. Several patients are currently being followed as their hyperthyroidism remains active. When these patients become euthyroid, repeat studies will be performed.

MR041.20.01-4001

ETIOLOGY OF HYPERCALCEMIA IN THYROTOXICOSIS. R.E. Reitz and R.L. Weinstein. Naval Hospital, Oakland.

The use of human parathyroid hormone (HPTH) in the radioimmunoassay (RIA) for parathyroid hormone has enabled us to measure metric amounts of HPTH in normal and hyperparathyroid subjects. Plasma HPTH and calcium (Ca) concentrations were similar throughout the day in normal subjects and no circadian variation was observed. Further, plasma HPTH varied inversely with serum Ca when hypercalcemia and hypocalcemia were induced.

HPTH concentrations were increased in primary hyperparathyroidism; Ca and EDTA (ethylenediamine tetraacetic acid) infusions were of no value in predicting the presence of adenoma or hyperplasia. The use of human hormone should facilitate the standardization and reporting of parathyroid hormone concentrations.

CICC 2-48-207

URINARY CYCLIC ADENOSINE MONOPHOSPHATE (CAMP) AFTER METHYLPREDNISOLONE IN THE BABOON. J. Sode, C.M. Herman, A. Ahmed and R. Johnsonbaugh. Naval Hospital and Naval Medical Research Institute, Bethesda.

The intracellular messenger CAMP can inhibit histamine release from leukocytes and has been shown to participate in some way in the immune responses of the organism. We investigated the effect of massive doses of methylprednisolone (MP) on the urinary CAMP excretion in seven adult baboons (*Papio doguera*). The animals were tranquilized with phencyclidine (Sernylan, 1.0 mg/Kg) for insertion of venous and urethral catheters, placed in a primate-restraining chair, and allowed to awaken. Three hours later a single intravenous dose of MP (3 mg/Kg) was administered. Urine samples were collected every two hours for measurement of CAMP by radioimmunoassay and creatinine (Cr) by autoanalyzer. Mean values \pm SEM for urinary CAMP were:

SAMPLE	CAMP (μ M/Gm. Cr)	p
Base line	4.45 ± 0.41	—
0-2 hours after MP	7.73 ± 1.23	< .05
2-4 hours after MP	7.15 ± 1.02	< .05
4-6 hours after MP	6.51 ± 0.84	< .05

A statistically significant change in urinary CAMP was not observed in a group of similarly prepared control animals. The intracellular sources contributing to the increase in urinary CAMP after MP are not known, but the observations are intriguing in light of recent reports that a strong immune signal for adenyl-cyclase activity may lead to inhibition of cellular events when superimposed on preexisting high activity of the enzyme.

CICC 2-06-322

IDENTIFICATION OF TREATABLE ETIOLOGICAL FACTORS IN OUTPATIENTS WITH IDIOPATHIC OSTEOPOROSIS. J. Sode, F. Nelson, W. Beckner and D. DeMaster. Naval Hospital, Bethesda.

Idiopathic osteoporosis is a common clinical problem and produces morbidity in 20% of the population above age 50 yrs. In an attempt to identify appropriate therapeutic modalities for individual patients, we studied 11 male and two female (mean age 63.1 yrs.) outpatients with idiopathic osteoporosis, according to a uniform protocol. All had significant axial osteoporosis and seven had vertebral fractures.

The fractions of ^{47}Ca absorbed and cleared from the plasma were determined by computer analysis of plasma-specific activity curves, seven-day body retention of ^{47}Ca by whole-body counter, and ionized serum Ca by ion-specific electrode. Serum total Ca, Mg, PO_4 , phosphatases, total protein, albumin and creatinine, as well as 24-hour urinary Ca, PO_4 and creatinine, were determined by standard methods.

The following etiological factors were identified: (1) Low dietary Ca intake, seven patients (pts); (2) Increased bone resorption, eight pts; (3) Low Ca absorption, 2 pts. The frequency of low dietary Ca intake was striking. Only three patients ingested normal amounts of Ca. The remaining had a mean Ca intake of 385 mg/day, and a mean absorption of 210 mg/day.

Osteoporosis, like anemia, does not have the specificity of a disease. The outpatient protocol devised permits identification of therapeutic modalities for individual patients, i.e. correction of dietary habits, vitamin D for decreased intestinal absorption of Ca, estrogens and/or Ca infusions for dominant bone resorption and oral phosphate for phosphate leaks.

CICC 2-06-325

SPIRONOLACTONE INHIBITION OF ADRENAL ANDROGEN SECRETION IN PATIENTS WITH METASTATIC CARCINOMA OF THE PROSTATE. P.C. Walsh, P.K. Siiteri, C.R. Sargent and M.B. Rotner. Naval Hospital, San Diego.

In this study, castrated men with carcinoma of the prostate have been treated with spironolactone in an attempt to induce remission of symptoms by inhibiting adrenal androgen production. Four men (46-66 years of age) with metastatic carcinoma of the prostate, who had previously been treated with estrogens and bilateral orchiectomy were studied. Base line blood samples were collected on three consecutive days prior to therapy; and then at one week (four men), two-three weeks (four men), and four-seven weeks (two men) after treatment with spironolactone, 400 mg/day. Plasma testosterone, androstenedione, and dehydroepiandrosterone were measured by a competitive enzyme method. Serum creatinine, electrolytes, acid phosphatase, and blood urea nitrogen determinations were also performed.

Plasma concentrations of testosterone, androstenedione, and dehydroepiandrosterone were significantly lower following therapy with spironolactone. This effect was more apparent after two-three weeks of treatment. Two patients experienced relief of pain. In one man, this was associated with decreased levels of serum acid phosphatase.

These data indicate that spironolactone suppresses adrenal androgen production and suggest that it may be of benefit in the treatment of orchiectomized patients with advanced carcinoma of the prostate. Spironolactone, additionally acting as an antiandrogen, may inhibit the effect of androgen at target tissues. CICC 3-16-187

SPLANCHNIC METABOLISM DURING CHRONIC STRESS IN ACTIVE DUTY PERSONNEL. R.L.

Weinstein and S.B. Lewis; Naval Hospital, Oakland.

H.V. Werner. University of California, San Francisco.

This project is designed to define the biochemical mechanisms which are altered during a simulated combat situation, e.g. the chronic stress of fasting. At the present time, CIC is setting up techniques for measurements of CO₂ tension. It is also performing preliminary studies to determine if the protocol may require alteration, because results of live enzyme and intermediary-metabolite studies, during starvation, have suggested that glucose metabolism by human liver may be nil after a 14-16 hour fast.

M4305.05-3073

MEASUREMENT OF GONADOTROPINS AND ANDROGENS IN PATIENTS WITH HYPOGONADISM.

R.L. Weinstein and R.E. Reitz. Naval Hospital, Oakland.

Gonadal and pituitary function have been studied in adult men and women with gonadal failure secondary to (a) primary defect in the testis or ovary, and, (b) hypothalamic-pituitary dysfunction. Measurement of serum gonadotropins (FSH and LH) have proved most useful in delineating these two etiologically distinct forms of gonadal failure. Undetectable or low serum FSH (<2 mIU/ml) or LH (<4 mIU/ml), in adult males or females clearly indicated hypothalamic-pituitary failure related to pituitary tumor, Sheehan's syndrome, or isolated gonadotropin deficiency. Elevated levels of serum FSH (>20 mIU/ml) or LH (>20 mIU/ml), in adult males or females clearly indicated primary gonadal pathology such as Klinefelter's syndrome, bilateral anorchia, bilateral mumps orchitis in the male and Turner's syndrome, pure gonadal dysgenesis, and premature ovarian failure in the female.

Measurement of plasma androgens (testosterone (T), androstenedione (A), and dehydroepiandrosterone (D)) was performed in males with both types of gonadal failure. The range and mean levels of plasma (A) and (D), in males with gonadal failure of whatever etiology (low or high serum gonadotropins), were not statistically

different from each other or from levels in normal adult males. However, in males with low serum gonadotropins, levels of plasma (T) were less than 0.10 µg% while in males with elevated serum gonadotropins, levels of plasma (T) ranged from 0.08-0.56 µg% (normal adult males, 0.28-1.20 µg%). The ability to simultaneously measure blood levels of gonadotropins and androgen has allowed better definition of the etiology of gonadal failure.

CICC 3-48-181

ANDROGENIC FUNCTION IN FEMALES WITH POLYCYSTIC OVARY SYNDROME. R.L. Weinstein and T.A. Daane. Naval Hospital, Oakland.

Plasma concentrations of testosterone, androstenedione and dehydroepiandrosterone were assayed in five subjects with polycystic ovary syndrome. Diagnosis was confirmed in all subjects at surgery. The purpose of this study was to determine whether wedge resection reduced androgen secretion in these patients and if, in fact, this was related to the resumption of their ovulatory cycles. Androgen levels were measured in these patients before and after dexamethasone suppression and during administration of human chorionic gonadotropin.

No significant difference in androgen levels was found following wedge resection in these patients. However, ovulatory cycles (evidenced by secretory endometrium on biopsy examination and basal body temperature charting) occurred in all five patients. The data obtained suggest that the resumption of ovulatory cycles in polycystic-ovary patients cannot be accounted for by a diminution in plasma androgen levels.

MR041.20.01-4001

MEASUREMENT OF GONADOTROPINS AND ANDROGENS IN PATIENTS WITH HYPOGONADISM.

R.L. Weinstein, Naval Hospital, Oakland; **and R.E.**

Reitz. University of California, San Francisco (UCSF).

A number of patients in whom the diagnosis of hypogonadism was established, were seen at Naval Hospital Oakland. Some have hypogonadotropic hypogonadism; others present hypergonadotropic hypogonadism, such as Klinefelter's syndrome. The purpose of the study is to determine which of these two types of hypogonadism is present, by measurement of serum gonadotropin levels in conjunction with plasma testosterone. With proper replacement therapy, active duty personnel could then be returned to full duty.

During the past year, work on this project has made it possible to define a global biosynthetic defect in the

Klinefelter testis that involves androgens (testosterone, androstenedione and dehydroepiandrosterone); estrogens (estradiol and estrones); and progestins (progesterone and 17-hydroprogesterone). Additionally, these data suggest that the gynecomastia observed in Klinefelter's subjects may be related to an increased estrogen-testosterone ratio vice absolute values of either circulating estrogens or androgens. Further, the Leydig-cell hyperplasia and nodule formation, seen on testicular biopsy examination in Klinefelter subjects, provide histologic evidence of this defective end-organ under the influence of elevated pituitary gonadotropins.

MR041.20.01-4001

STUDY OF HYPOGONADOTROPIC HYPOGONADISM: PHASE II. R.L. Weinstein, Naval Hospital, Oakland; and R.E. Reitz. UCSF.

A family of nine siblings, four of whom demonstrate isolated gonadotropin deficiency with unique neuroendocrine variants, were investigated. The striking data obtained reveal that decreased secretion of gonadotropins (FSH and LH) in these subjects is due to a deficiency of hypothalamic (gonadotropin) releasing factors.

MR041.20.01-4001

MINERALOCORTICOID EXCRETION IN HYPERTENSIVE STATES IN PATIENTS SEEN IN MILITARY HOSPITALS. R.L. Weinstein, Naval Hospital, Oakland; and R.E. Reitz. UCSF.

Mineralocorticoid excretion of aldosterone, corticosterone (tetrahydrocorticosterone) and deoxycorticosterone (tetrahydrodeoxycorticosterone) has been measured by a double isotope derivative technique combined with gas liquid chromatography. Age-matched normotensive and hypertensive male subjects were studied on normal (100 mEq sodium), low (10 mEq sodium), and high (210 mEq sodium) salt intake. In addition, normotensive and hypertensive subjects were studied before and after dexamethasone suppression. Red cell and plasma volumes were determined utilizing the ⁵¹Chromium radioisotope technique. Formulation of this data has been completed and a paper has been prepared for publication.

The data obtained indicate that mineralocorticoid excretion during varied salt intake and dexamethasone suppression, in hypertensive subjects, is comparable to that demonstrated in normotensive subjects. Moreover, the statistically significant contracted plasma

volume found in the hypertensive subjects seems to have no influence on the pattern of mineralocorticoid excretion in essential hypertension.

MR041.20.01-4001

CALCIUM-PARATHYROID INTERRELATIONSHIPS IN CHRONIC RENAL DISEASE. R.L. Weinstein, Naval Hospital, Oakland; and R.E. Reitz. UCSF.

It is well known that patients with chronic renal failure have secondary hyperparathyroidism. The mechanism for this is not clear, although abnormalities in vitamin D metabolism and/or phosphate retention may play a role in this disorder. It is now known that the radioimmunoassay currently available for parathyroid hormone (PTH), although capable of measuring known amounts of human hormone in plasma, is unable to distinguish among the smaller molecular weight peptides that circulate in the plasma of patients with chronic renal disease. It is therefore of paramount importance that an antiserum which will detect only the biologically active portion of the PTH molecule, that is the amino-terminal portion, be developed. At the present time an immunization program utilizing bovine PTH injections into guinea pigs is underway. In the meantime, changes in hormone concentration, although relative rather than absolute values, can be determined by currently available procedures.

Future plans include the preparation and characterization of an antiserum, specifically for the biologic portion of the parathyroid-hormone molecule, and measurement of changes in hormone concentration in patients with chronic renal failure utilizing this particular system. Employing these techniques, one can then accurately predict the optimal concentration of calcium in the dialysate for reduction in parathyroid hormone secretion in these patients.

MR041.20.01-4001

EVALUATION OF THE ROLE OF THYROTROPIC HORMONE IN SIMPLE AND MULTINODULAR GOITER AND THYROID CARCINOMA. G.J. Weir, Jr. Naval Hospital, Great Lakes.

Assay of thyrotropin (TSH) should aid in diagnosing hypothyroidism and in following thyroid carcinoma. This study will develop a radioimmunoassay for TSH and evaluate its clinical use. Samples of TSH for labeling and standardization, and of anti-TSH have been obtained from the National Institutes of Health. Six attempts have been made to iodinate TSH samples using the standard iodination procedure of oxidation with chloramine-T.

To date the iodination procedure has not been successful. Separation of the labeled material utilizing Sephadex chromatography has resulted in uniform spread of radioactivity instead of the expected double peak. An alternate method of iodination is currently being evaluated.

CICC 2-13-013

KETONE-BODY PRODUCTION BY LIVER AND UTILIZATION BY SKELETAL MUSCLE DURING STARVATION. H.V. Werner. Naval Hospital, Oakland.

Fat mobilization is markedly increased during stress, e.g., combat, exercise, starvation; in man a varying degree of ketosis follows. Overproduction of acetoacetate and beta-hydroxybutyrate by the liver is thought to be the cause. Recent findings in this laboratory suggest that a sensitive control of ketone-body utilization is located in the periphery: 1) Acute inhibition of fat mobilization by niacin in starved humans is not followed by a similar decrease in ketones; 2) Post-exercise ketosis in normal males persists for two hours after fat mobilization ceases; and 3) Despite elevated free fatty acids, ketosis is not present in dogs or rabbits fasted up to two weeks. If the peripheral utilization of ketone bodies is an important control site, prophylaxis or therapy could be directed at this point.

At laparotomy, polyethylene catheters are placed in the portal and hepatic veins of the dog and led to the dorsal surface via the rib cage. The catheters are maintained patent by use of heparin (100 USP units/ml) plug until full recovery is evident (10-14 days). Blood (femoral artery; and portal, hepatic and femoral veins) is drawn in the post-absorptive state and after 72 hours of fast, while blood flow through the liver and lower limb is measured by indocyanine green and Evans blue dye. Rates of production and utilization of acetoacetate and beta-hydroxybutyrate are calculated on the basis of differences in the concentrations of these metabolites entering and leaving these tissues. This study will proceed when the conclusions resulting from a study of metabolic effects of liver injury are available.

MR041.20.01-0378

GLUCONEOGENESIS IN ISOLATED LIVER PARENCHYMAL CELLS FROM FASTED OR FROM FED RATS. H.V. Werner. Naval Hospital, Oakland.

The synthesis of carbohydrate from endogenous precursors supplies the body with glucose when the diet is deficient in carbohydrate. Consequently an ample dietary supply of carbohydrate could minimize the need for gluconeogenesis, while starvation might maximize

hepatic gluconeogenic capacity. Supportive evidence for this concept has been obtained and the findings have been interpreted to indicate that, in fasted rats, hepatic gluconeogenic capacity is enhanced; the mechanism for this is an increased level of rate-limiting enzymes, allowing increased substrate flux to glucose.

Enzyme activities of glucose-6-phosphatase, fructose-1,6-diphosphatase, pyruvate carboxylase and phosphoenolpyruvate carboxykinase were measured in isolated cells. To determine whether hepatic gluconeogenic capacity is increased in fasted rats, and, if so, its mechanism of stimulation, rates of glucose production from exogenous lactate, pyruvate, fructose, sorbitol, dihydroxyacetone or glycerol were also measured in cells from fasted and from fed animals. Only lactate flux to glucose was increased in cells from fasted animals. The mechanism of this stimulation was studied by using agents which stimulate rates of gluconeogenesis from pyruvate or lactate.

It was concluded that pyruvate carboxylase and phosphoenolpyruvate carboxykinase did not limit basal rates of gluconeogenesis but became limiting factors only in the stimulated state. By using fluorodicarboxylic acids, the stimulation of lactate metabolism via fasting was further defined as an enhanced translocation of the oxaloacetate carbon skeleton out of the mitochondria.

MR041.20.01-0383

GLUCOSE-ATP-6-PHOSPHOTRANSFERASES OF ISOLATED RAT LIVER PARENCHYMAL CELLS. H.V. Werner, J.C. Bartley and M.N. Berry. Naval Hospital, Oakland.

Rat liver contains four glucose-ATP-6-phosphotransferases. Three of these enzymes, termed hexokinase (EC 2.7.1.1), have a high affinity for glucose ($K_m = 10^{-4}$ to 10^{-6} M) and are unaffected by starvation. Glucokinase (EC 2.7.1.2), the fourth enzyme, has a high K_m (10^{-2} M) and decreases in activity after fasting. The distribution of these enzymes throughout the liver has important implications for parenchymal cell carbohydrate metabolism. While glucokinase is an enzyme of the hepatocyte, the cellular locus of the hexokinases is less certain.

Hexokinase content of isolated rat liver parenchymal cells was determined by spectrophotometry, column chromatography and electrophoresis. Spectrophotometric data indicated the presence of significant hexokinase in the isolated rat liver parenchymal cells. Separation of the glucose-ATP-6-phosphotransferase activity into specific isoenzymes confirmed that the hepatocyte definitely contains hexokinase. In rats fasted

one to seven days, there was no change in the hexokinase activity in hepatocytes or in whole liver, while glucokinase in both preparations was markedly decreased. Hexokinase and glucokinase activities in whole liver from starved animals were similar.

The data clearly indicate that rat liver parenchymal cells contain both an adaptive enzyme, i.e., glucokinase; and constitutive enzymes, i.e., the hexokinases, which phosphorylate glucose. Because of the cellular heterogeneity of rat liver, comparison of isoenzyme activities in whole liver homogenates can indicate accurate parenchymal cell levels only if the measured enzymes have a similar distribution in the non-parenchymal cells.

MR041.20.01-0390

REDUCING EQUIVALENT TRANSFER ACROSS LIVER MITOCHONDRIAL MEMBRANES: STIMULATION BY THYROXINE IN RATS. H.V. Werner and M.N. Berry. Naval Hospital, Oakland.

Shuttles for transferring reducing equivalents between cell compartments are rate-limiting and may be sites of hormone action (Berry and Kun, *Eur. J. Biochem.* 27: 395, 1972). Accordingly, reducing equivalent flux was determined by measuring substrate removal, metabolite accumulation and oxygen consumption in the metabolism of pyruvate, sorbitol, or glycerol in isolated liver parenchymal cells from control ($n = 26$) and from l-thyroxine ($n = 15$) treated rats.

Transfer to cytoplasm of reducing equivalents generated in pyruvate oxidation in mitochondria increased from 2.43 ± 0.11 to 4.07 ± 0.21 ($\mu\text{moles/min/gm}$, mean \pm SEM) in cells from treated rats. Transfer to mitochondria of reducing equivalents generated in cytoplasm was also enhanced: in sorbitol oxidation, flux increased from 1.81 ± 0.09 to 2.43 ± 0.07 , while in glycerol oxidation reducing equivalent transfer to oxygen increased from 1.61 ± 0.05 to 3.11 ± 0.19 . Flux from sorbitol and glycerol (incubated together) was elevated threefold, from 1.57 ± 0.07 to 4.60 ± 0.21 . Studies with specific inhibitors of the shuttles (by fluorodicarboxylic acids), and of the electron transport chain (by rotenone or antimycin A), indicated that the flux of reducing equivalents generated in pyruvate metabolism was enhanced by the malate-oxaloacetate shuttle, while those in sorbitol and glycerol metabolism were enhanced via the α -glycerophosphate shuttle.

Conclusions: 1) Thyroxine enhances reducing-equivalent flux; 2) Increased metabolism of hyperthyroidism may result from stimulation of these rate-limiting shuttles.

MR041.20.01-0383

GASTROENTEROLOGY

CORRELATION OF PORTAL HEMODYNAMIC ABNORMALITIES WITH THE SEVERITY OF CHRONIC LIVER DISEASE. D.O. Castell and J.P. Kirchner.

Naval Hospital, Philadelphia.

Recent studies have indicated that radioactive xenon gas can be utilized as a functional test of portal circulatory dynamics by monitoring the time required for rectally-administered xenon to appear in the heart blood. The present studies were undertaken to further delineate the relationship of the xenon "rectum-to-heart time" to the portal flow.

Preliminary studies on six intact animals have shown the normal "rectum-to-heart time" in adult dogs to range from 6-14 sec. Additional studies of portal flow, utilizing an indwelling thermal catheter specifically designed for this study to measure flow in the portal vein, have yielded results consistent with those previously found by other techniques. Following the surgical creation of portal hypertension and portacaval anastomosis, xenon studies will be repeated. Comparison is being made between the measured circulation time and the portal hemodynamics measured directly in these animals. An attempt will be made to utilize this basic experimental information to further apply the xenon circulation time as a functional test of liver portal hemodynamics in patients with hepatic disease. Studies are in progress.

CICC 2-05-601

ILEAL REFLUX AFTER GASTRIC ALKALINIZATION. D.O. Castell and G. Jervey. Naval Hospital, Philadelphia.

The recent observation that the gastrointestinal hormone gastrin causes relaxation of the human ileocecal sphincter suggested the possibility of stimulation of endogenous gastrin as a mechanism to increase reflux of barium-contrast material from the cecum into the terminal ileum. We have studied this effect in the Radiology Unit by a randomized blinded approach, in patients in whom routine barium enema failed to attain visualization of the terminal ileum.

The patients received randomly 60 ml of either water or antacids by mouth, and were then reexamined blindly by the radiologist, looking for reflux of barium from cecum to terminal ileum. Studies were performed in 21 consecutive patients. The only patients to reflux barium subsequent to their treatment were three out of the 13 in the antacid group. None of eight patients in the control group (water) showed

reflux. These results were not statistically significant (Chi square = 2.5; $p > 0.1$).

These observations would indicate that simple gastric alkalization will not result in the high frequency of positive reflux of barium into the terminal ileum that is desired. It is conceivable that when synthetic pentagastrin becomes readily available for clinical use, further studies using this drug might prove rewarding. CICC 2-05-606

EVALUATION OF ACUTE DIARRHEAL STATES IN THE MILITARY POPULATION. A.R. Chappelka and M.D. Dickman. Naval Hospital, Philadelphia.

The microflora of the alimentary tract of 20 normal subjects and 80 samples from patients with acute and chronic diarrheal disease have been compared. Low numbers of microorganisms (mean: $10^{1.8}$) including streptococci, lactobacilli, yeast, and *Veillonella* were consistently isolated from the small bowel of the normal subjects, and apparently represent remnants of the salivary microflora surviving the gastric barrier.

Higher numbers of these organisms (mean: $10^{3.8}$), as well as some unusual isolates (e.g. coliforms and *Staphylococcus aureus*) were recovered from the small bowel of patients during the acute phase of diarrheal disease but were absent during convalescence. Data fail to implicate any particular agent, suggesting that these changes are nonspecific sequelae of the acute episode. Patterns of microflora observed in the small bowel of patients with chronic diarrheas of varying etiologies appear related and are best visualized as a continuum. Patients with symptoms of chronic diarrhea of unknown etiology, with underlying pathology, or following surgical procedures (in that order) exhibit increases in the: numbers of organisms, complexity of microflora, and colonic isolates at the ligament of Treitz. The reversal in the *Bacteroides*/coliform ratio reported in the feces of patients with diarrhea of known etiology appeared in only 20% of the cases studied. The numbers and types of *Enterobacteriaceae* in adult and pediatric patients, at the acute phase differed from findings at convalescence. Currently these changes in the fecal and small-bowel microflora of patients with naturally occurring acute episodes are being further evaluated with artificially induced diarrheas in this laboratory.

MR041.20.01-0372

SIGNIFICANCE OF ABNORMAL LIVER FUNCTION STUDIES IN PSYCHIATRIC ADMISSIONS TO MILITARY HOSPITALS. A.R. Chappelka and R.L. Farrell. Naval Hospital, Philadelphia.

A pilot study at the Naval Hospital Philadelphia revealed that approximately one-third of the psychiatric admissions presented with abnormal liver function studies. To ascertain the clinical significance of this observation 300 admissions were evaluated by questionnaire as to liver disease and liver function studies, including Australia antigen. If the questionnaire revealed significant data or the liver function studies were abnormal, the patient was further evaluated and, in those cases where clinically indicated, liver biopsy was obtained. Correlation with tours in Vietnam, alcoholic consumption, and illicit and therapeutic drug usage was determined.

As predicted from the pilot study, one-third of the patients had abnormal liver function studies. Of this group, 20% received liver biopsy. Significant pathology was detected in virtually all biopsies; "hippie hepatitis" and persistent hepatitis were the predominant findings. Follow-up study of the group has begun to determine the long-term outcome and the advisability of medical therapy such as steroids. It was apparent that the history, transaminase determinations and liver biopsy were the more rewarding parameters of investigation, and that accurate appraisal was not possible without biopsy examination.

MR041.20.01-0403

THE EFFECT OF ALCOHOL ON THE FINE STRUCTURE OF MOUSE GASTRIC MUCOSA. G.L. Eastwood and J.P. Kirchner. Naval Hospital, Philadelphia.

The ultrastructural changes in the gastric mucosa produced by ethyl alcohol (EtOH) have not been well studied. We examined the gastric mucosa of 75 fasted mice by light and electron microscopy. Except for three non-intubated controls, each group of three mice received, via esophageal intubation, one of the following solutions for two, five or 15 minutes: 145 mN (millinormal) NaCl, 25% EtOH, 25% EtOH + 100 mN HCl, 25% EtOH + 10 mN HCl, 10% EtOH, 10% EtOH + 100 mN HCl, 10% EtOH + 10 mN HCl, 45 mN NaCl + 100 mN HCl.

By light microscopy, 25% EtOH, both with and without HCl, and 10% EtOH with HCl produced surface epithelial damage by as early as two minutes in some animals. By electron microscopy, a gradient of EtOH-induced lesions was observed. First, the nuclear chromatin of surface mucous cells became clumped, often associated with cytoplasmic vacuolization, loss

of ground substance, and distortion of mitochondria. In more severe lesions the apical cell membrane became distorted and broken. Finally, cells fragmented and sloughed off. Apical mucin granules appeared normal until dispersed by cellular disruption. Throughout this sequence of injury, tight junctions remained intact and cells cleaved, often without regard to cell boundaries. These studies indicate: (1) EtOH can produce gastric mucosal damage in the mouse within two minutes. (2) The initial lesion involves intracellular changes in the surface mucous cells. (3) Tight junctions remain apparently intact throughout the sequence of mild-to-severe damage to surface epithelial cells.

CICC 3-05-194

STIMULATION OF THE INCOMPETENT LOWER ESOPHAGEAL SPHINCTER. A POSSIBLE ADVANCE IN THERAPY OF HEARTBURN. R.L. Farrell and D.O. Castell. Naval Hospital, Philadelphia.

The primary function of the lower esophageal sphincter (LES) is to prevent the reflux of gastric contents into the esophagus. We have studied the effect of hormonal and pharmacologic stimuli on LES pressure in patients with symptomatic gastroesophageal reflux due to LES incompetence. Gastric alkalization, subcutaneous pentagastrin, intravenous edrophonium, and subcutaneous bethanechol each resulted in marked increases in LES pressure. In all studies pressure rose to a level occurring in normal subjects.

Subsequently the patients were given 25 mg bethanechol orally, and pressure was monitored for two hours. LES pressure increased from a mean basal measurement of 5.6 ± 0.8 mm Hg, to a peak of 16.9 ± 2.8 mm Hg at 50 minutes. Pressure remained elevated for the full two-hour study period. Both subcutaneous and oral bethanechol successfully increased LES pressure in all patients with symptomatic reflux to the level of resting pressure seen in normal subjects.

These studies suggest a potential role for cholinergic agents in therapy of symptomatic gastroesophageal reflux. A randomized, double-blinded, controlled clinical trial with bethanechol in patients with chronic heartburn is currently in progress.

MR041.20.01-0321

COLONOSCOPY IN THE EVALUATION OF PATIENTS WITH HEMATOCHESIA. M. Fornes and O. Nebel. Naval Hospital, San Diego.

We have found colonoscopy to be useful in the evaluation of suspicious or questionable barium enema findings and are currently studying its use in evaluation

of colonic hemorrhage. To date ten consecutive patients with hematochezia have been evaluated by colonoscopy. One patient, thought to have carcinoma of the colon on barium enema, was found to have Crohn's colitis above the reach of the sigmoidoscope, and one patient thought to have a large pedunculated polyp on barium enema, was found to have only diverticulosis on colonoscopy and repeat barium enema.

Our initial experience with colonoscopy indicates that it is a valuable adjunct in the evaluation of patients with hematochezia. In addition, preliminary experience with colonoscopy in the evaluation and removal of colonic polyps suggests that this technique will provide a new approach to the treatment of this problem. Finally, collaboration between the GI Branch at this facility and NAMRU 3 in Cairo, Egypt, in the colonoscopic evaluation of schistosomal polyposis, has produced convincing data to show that this condition is amenable to medical treatment and that colectomy is generally not indicated in these critically ill patients.

CICC 3-16-053

EXAMINATION OF THE DESCENDING COLON WITH THE FIBEROPTIC COLONOSCOPE. G.E.

Gorsuch and G.T. Roling. Naval Hospital, Oakland.

During the eight months the Gastroenterology Branch at Naval Hospital, Oakland has utilized the fiberoptic colonoscope, 26 patients have undergone colonoscopic examination. In 18 an attempt was made to pass the scope its entire length of 187 cm. This was accomplished in only one patient; an average distance of 120 cm was reached in this group. Eight patients had sigmoid pathology preventing the passage of the scope beyond this area. In seven of the 26 patients, "roentgenographic lesions" were demonstrated but colonoscopic examinations were unremarkable. Of the 26 patients, six demonstrated colon pathology but their barium enemas were within normal limits. In addition, a total of six polyps were not detected on barium enema. The polyps averaged about 5-8 mm in size; none exceeded 1 cm in size. Surgical therapy of presumed lesions was obviated in seven patients, either by a change in diagnosis on the basis of findings at colonoscopy, or a failure to find roentgenographic abnormalities. Demonstration of polypoid disease by colonoscopy complemented a roentgenographic study of the large bowel.

Our preliminary findings with the use of this instrument suggest that colonoscopy may form an integral part of the preoperative evaluation of these patients, and that exploratory laparotomy will seldom be

necessary to accurately define a colonic lesion. With improvements in technique, examination of the total colon is feasible and should require little additional time.

CICC 2-48-220

THE SIGNIFICANCE OF AUSTRALIA ANTIGENEMIA IN APPARENTLY HEALTHY BLOOD DONORS.

F.M. Griffin, Jr. Naval Hospital, Great Lakes.

In an effort to determine the significance of Australia antigenemia in apparently healthy blood donors, twelve asymptomatic male recruit trainees with Australia antigenemia were evaluated by history and physical examination, biochemical tests of hepatic function, and percutaneous hepatic biopsy. All were entirely well on physical examination. Nine of the 12 men had normal liver function studies; three had enzyme elevations. On biopsy, five specimens were normal; seven specimens revealed changes consistent with a diagnosis of viral hepatitis. No patient had persistent limiting-plate disruption, cirrhosis, or hepatic steatosis.

Asymptomatic Australia antigenemia and abnormal biochemical tests of hepatic function do not constitute a sufficient indication for hepatic biopsy. Rather, the patient can be followed clinically; biopsy need be performed only if evidence of persistent hepatic inflammation or chronic liver disease develops.

CICC 2-13-007

EVALUATION OF INTESTINAL ABSORPTION IN VIRAL HEPATITIS. **R.H. Higgs and A.R. Chappelka.** Naval Hospital, Philadelphia.

Fifteen cases of acute viral hepatitis were evaluated to determine if there is an associated malabsorptive state. Serum carotene, D-xylose excretion, and the Triglyceride Tolerance Test were the parameters employed.

The serum carotene levels and the D-xylose excretions showed no significant difference from normal controls. The Triglyceride Tolerance Test revealed erratic results which could not be correlated with the clinical picture. Fecal fat determinations (to evaluate these erratic results) were not carried out for fear of transmitting hepatitis.

In conclusion: (1) No evidence of malabsorption was demonstrated in acute viral hepatitis using the serum carotene and D-xylose excretion tests. (2) The Triglyceride Tolerance Test is probably invalid in acute liver disease.

CICC 2-05-605

THE EFFECT OF MONOAMINE OXIDASE INHIBITION ON EXPERIMENTAL CIRRHOSIS. **J.P.**

Kirchner, L.M. Davis and D.O. Castell. Naval Hospital, Philadelphia.

Elevation of serum monoamine oxidase (MAO) levels in patients with cirrhosis suggests a possible role for this enzyme in the formation of fibrosis. We have studied the effect of MAO inhibition on experimental cirrhosis in rats.

All animals received 50% carbon tetrachloride (CCl_4) in corn oil, 1.3 ml/kg twice weekly and: either no additional drug (Group I), or D-Penicillamine (Group II), or nialamide (Group III). Control rats for each of the above groups received no CCl_4 . After 14 weeks of therapy the rats were sacrificed; cirrhosis was evaluated, both histologically and by liver-hydroxyproline content. The CCl_4 -treated rats all presented coarse-nodular cirrhosis but fibrosis was more apparent histologically in Group III. Mean liver hydroxyproline content was $817 \pm 114 \mu\text{g/g}$ (\pm SE) in Group I and $1033 \pm 116 \mu\text{g/g}$ in Group II. These values are not significantly different. For Group III mean hydroxyproline content was $1545 \pm 184 \mu\text{g/g}$, which is significantly greater than that obtained for Group I ($p < 0.01$), or Group II ($p < 0.05$).

These observations indicate that MAO inhibition results in increased cirrhosis secondary to CCl_4 treatment.

MR041.20.01-0392

COFFEE: TRICK OR TREAT? **David M. McCance, Raymond B. Johnson and William M. Lukash.** Naval Hospital, Bethesda.

Consumer research shows that coffee remains the most popular beverage in this country. Its features of pleasant taste, production of euphoria and an increased alertness have resulted in its universal acceptance as a way of life. An average of 16 pounds of coffee per person is consumed annually in the U.S. Our seagoing Navy *doubles* that figure. Since caffeine, the primary active ingredient in coffee has known specific pharmacologic effects on gastric secretory function, a study was initiated to investigate the effect of coffee on this secretory function.

A modified caffeine gastric analysis was performed on 12 normal volunteers. Each subject underwent five separate tests with determination of gastric acid output following: 1) 100 mg Histalog; 2) 75 mg caffeine sodium benzoate; and 3) three different brands of instant coffee, each containing 75 mg caffeine. Basal acid output was first measured in each subject, followed by the above-noted studies.

The results indicated that the 75 mg of caffeine present in an average cup of instant coffee is a modest stimulant for acid secretion. Considering the magnitude of coffee consumption and its known pharmacologic effects, further studies would seem warranted to determine the possible relationship of this beverage to the problem of peptic ulcer disease.
CICC 3-06-127

DUODENOSCOPY AND THE DIAGNOSIS OF UPPER GASTROINTESTINAL BLEEDING. O.T. Nebel and D.O. Castell. Naval Hospitals, San Diego and Philadelphia.

Despite a vigorous diagnostic approach using barium-contrast radiography and fiber-esophagogastrosocopy, the site of acute upper gastrointestinal (UGI) bleeding remains undiagnosed in 7-25% of patients. This study was designed to determine if the recently developed fiberoendoscopy (Olympus-JF) would aid in the diagnosis of patients presenting UGI hemorrhage. Fifty patients with acute UGI bleeding were evaluated within 24-48 hours by barium contrast radiography, esophagogastrosocopy, and duodenoscopy. The mean age of the patients was 47 years, and 65% were veterans or retired military personnel.

A pathologic lesion to which the bleeding could be attributed was found in all patients. These lesions included gastritis (32%), duodenal ulcer (30%), gastric ulcer (16%), Mallory-Weiss syndrome (10%), esophageal varices (8%), and erosive esophagitis (4%). Nine (18%) patients had lesions that could have been the source of UGI bleeding but were not the site of acute bleeding. Duodenoscopy was the only positive diagnostic procedure in seven (14%) patients.

These data indicate that duodenoscopy should be performed on all patients with UGI bleeding because of the frequent occurrence (14%) of radiographically unrecognized duodenal ulceration.

CICC 3-16-046

SCHISTOSOMAL POLYPOSIS: ENDOSCOPIC AND HISTOLOGIC EVALUATION OF MEDICAL THERAPY. O.T. Nebel, D.O. Castell, N. Ayad, Z. Farid and H.A. Sparks. Naval Hospital, Philadelphia and NAMRU No. 3 Cairo, Egypt.

In highly endemic areas, colonic polyps are a common complication of schistosomiasis (S). Extensive polyposis may occur with significant morbidity and mortality. Niridazole has been shown to be an effective therapeutic agent possibly associated with polyp regression. The purpose of this study was to

determine, by colonoscopy and biopsy, the effect of medical therapy in patients with S polyposis.

Fifteen patients with S colonic polyposis, documented by barium enema and colonoscopy, were evaluated prior to treatment. All patients had viable S eggs in the stool and on polyp biopsy. Clinical presentation was characterized by a long history of S with several months of diarrhea and hematochezia. Hepatosplenomegaly was a common physical finding and laboratory examination revealed anemia, in addition to abnormal liver function studies. After treatment with niridazole, all 14 patients have shown marked improvement in physical status, laboratory studies, barium enema and colonoscopy. The innumerable, fungating, necrotic, polypoid masses seen on initial examination have gradually regressed, while stool cultures and colonic biopsy show no viable eggs. Examination of post-treatment rectal biopsy revealed no significant histologic abnormalities.

These data support the efficacy of medical therapy in the treatment of S polyposis and indicate that the polyposis may be a reversible lesion.

MR041.20.01-0348

ENDOSCOPIC PANCREATOCHOLANGIOGRAPHY.

O.T. Nebel and M. Fornes. Naval Hospital, San Diego.

We have evaluated our experience in performing 50 endoscopic pancreatocholangiograms (EPC). In addition, preliminary data on the use of this technique in the evaluation of patients with obstructive jaundice and recurrent pancreatitis has been reviewed.

Analysis of the last 20 cases reveals that we were successful in obtaining pancreatograms in 14 out of 15 attempts (93%) and cholangiograms in 4 out of 5 attempts (80%). We have experienced no significant complications from the procedure although postpancreatogram hyperamylasemia was seen in 7 out of 13 (52%) patients. An increase in amylase of 404 ± 190 units (mean \pm SEM) occurred six to eight hours following the procedure. To date, ten patients with recurrent pancreatitis have been evaluated by EPC. Pancreatography in four of these patients showed mild to marked deformity of the main pancreatic duct, with stenosis and poststenotic dilatation. In five patients with obstructive jaundice, endoscopic cholangiogram was helpful in localizing the site and type of biliary obstruction. One case of hepatoma presented a normal biliary tree and three cases of common duct stone were diagnosed by this technique.

Our initial experience with endoscopic pancreatocholangiography indicated that it is a safe, effective

diagnostic procedure that may be helpful in the evaluation of selected patients with pancreatobiliary disease. CICC 3-16-029

DETERMINANTS OF LOWER ESOPHAGEAL SPHINCTER PRESSURE. O.T. Nebel and M. Fornes. Naval Hospital, San Diego.

We have no data on this project and are awaiting the arrival of the manometry system. It is anticipated that work will begin shortly after the first of the year. Esophageal mucosal changes produced by esophageal reflux will be studied in patients with symptomatic esophageal reflux and lower esophageal sphincter incompetency, as defined by a lower esophageal sphincter pressure of less than 10 mm of mercury. These patients will be studied with esophagoscopy and biopsy, and compared with a group of asymptomatic patients. In addition, further studies on the effect of various foods on the lower esophageal sphincter will be carried out, to determine if the previously demonstrated changes in lower esophageal sphincter strength produced by a variety of "pure" foods is clinically significant.

CICC 3-16-157

EVALUATION OF THE DIAGNOSTIC ACCURACY OF THE OLYMPUS GIF PANENDOSCOPE IN UPPER GASTROINTESTINAL DISEASES. J.Q. Stauffer. Naval Hospital, Great Lakes.

Upper gastrointestinal (UGI) endoscopic procedures have been performed 225 times on 205 patients during the preceding 12 months. All patients had clinical symptoms suggesting active UGI disease. The predominant endoscopic findings were correlated with the radiologic findings and clinical course, to evaluate the usefulness of routine esophago-gastroduodenoscopy.

Diseases of the distal esophagus were the predominant endoscopic abnormality encountered (90/225; 40%). In patients with superficial esophagitis (51/225; 22.7%), the radiological examinations were uniformly negative except for demonstration of a hiatal hernia. There were 15 cases (6.7%) with biopsy-proven esophagitis, without a demonstrable hiatal hernia. The clinical symptoms and response to therapy correlated well with the endoscopic findings. Gastrosocopy confirmed the presence of active gastritis (25/225; 11.1%) where X-ray examination was non-diagnostic. With extensive antral scarring (20/225; 8.8%), the added benefit of endoscopy was that biopsies were taken and examined for malignancy. Duodenoscopy was also helpful in detecting superficial ulcerations (13/225; 5.8%). In

patients with bleeding duodenal ulcers (12/225; 5.3%), endoscopy and radiologic examinations supplemented each other. Posterior duodenal bulb ulcers could not be visualized in three cases, but there was sufficient duodenitis present to make an endoscopic diagnosis. In five cases active bleeding from the duodenum was seen, while the UGI series was non-diagnostic.

CICC 2-13-005

HYPEROXALURIA IN PATIENTS WITH REGIONAL ENTERITIS AFTER ILEAL RESECTION. J.Q. Stauffer. Naval Hospital, Great Lakes.

Patients with regional enteritis and resection of the terminal ileum have an increased incidence of urolithiasis. Some of these patients have elevated rates of urinary oxalate excretion (UoxV), thought to be related to abnormal bile-salt metabolism. We have studied ten patients with regional enteritis. Group (Gp) A consisted of five patients with minimal or no resection of terminal ileum (mean 9.5 cm). Gp B consisted of five patients with resection of terminal ileum, from 30 to 150 cm (mean 65 cm); one had a calcium-containing renal calculus. Basal UoxV was normal in Gp A (13.9 ± 1.1 mg/24 hr; normal = 9-39 mg/24 hr), but was elevated in Gp B (48.0 ± 6.9 mg/24 hr; $p < .02$). Cholestyramine (ChS), a drug which binds bile salts, was given orally 16 gm/day; UoxV fell promptly in Gp B to 25.9 ± 4.1 mg/24 hr ($p < .05$), but remained unchanged in Gp A at $16.2 \pm .9$ mg/24 hr ($p > .20$); the difference between the two groups was no longer significant. An additional patient with an ileostomy following a 40 cm ileal resection had a normal UoxV. Four patients in Gp B had severe diarrhea which responded promptly to ChS medication.

These data suggest that increased UoxV occurs only in patients with ileal resections greater than 30 cm, and that this correlates with the clinical symptoms of explosive watery diarrhea. Reversal of the increased UoxV and the bile salt-induced diarrhea with ChS suggests that it is the delivery of abnormal quantities of bile salt into the colon which leads to an increased UoxV. Failure of the patient to develop hyperoxaluria, following a 40 cm resection with ileostomy also supports this hypothesis. ChS corrects the hyperoxaluria and the bile-salt diarrhea.

CICC 2-13-010

HYPERALIMENTATION. G.A. Ulch. Naval Hospital, Great Lakes.

The purpose of this study has been to measure various laboratory parameters while subjects are receiving

parenteral hyperalimentation. Each patient has been evaluated by multiple laboratory parameters before, during, and after institution of hyperalimentation. During the year 1972, 16 patients were studied. The length of hyperalimentation ranged from two to 33 days. The majority of patients had abdominal problems or complications which required total parenteral hyperalimentation.

The most striking laboratory findings involved the alkaline phosphatase and serum glutamic oxalic transaminase measurements, both of which were elevated in patients receiving treatment for more than seven days. No appreciable change was noted in the serum albumin and hematocrit levels in spite of improved nitrogen balance. Weight gain has been minimal or absent in those receiving hyperalimentation for less than two weeks. One patient on hyperalimentation for 33 days had a weight increase of only six pounds, in spite of a total caloric intake of 4000. No significant aberrations were noted in the serum magnesium levels. It is hoped to eventually expand the program to include measurement of other trace elements. The complications have been few and include pneumothorax and *Candida* sepsis.

CICC 2-13-001

HEMATOLOGY

STUDY OF COAGULATION SYSTEM IN PATIENTS WITH CHRONIC HYPOXIA. R.A. Burningham and J.E. Engeler, Jr. Naval Hospital, Philadelphia.

A severe bleeding diathesis was recently noted and studied at this hospital in a patient with chronic hypoxia secondary to chronic obstructive lung disease. The clinical course and laboratory data indicated a severe disseminated intravascular coagulopathy (DIC). None of the usual causes for DIC could be found. The present study was designed to investigate coagulation mechanisms in patients with chronic hypoxia.

All patients admitted to the Medical Service with known cardiopulmonary disease and an arterial PO_2 of less than 88 mmHg at rest will be studied. The following tests will be performed: complete blood count, platelet count, bleeding time, prothrombin time, non-activated partial thromboplastin time, Stypven clotting time, thrombin time, fibrinogen level, serial protamine sulfate dilution test, fibrin degradation products, platelet retention test and platelet aggregation.

Appropriate controls were established for each of the determinations listed. Fourteen patients with arterial

PO_2 of less than 80 mmHg were studied. A complete set of studies is available in five out of the 14 patients. No abnormalities were noted in these five patients.
CICC 2-05-608

LYSOZYME ACTIVITY IN VARIOUS BIOMEDICAL DISORDERS. R.A. Burningham and J.E. Engeler, Jr. Naval Hospital, Philadelphia.

The purpose of this study was to determine the serum lysozyme activity in a wide variety of hematologic and non-hematologic conditions. Serum samples were collected from patients referred to the Hematology and Medical Oncology Branch.

Out of 259 initial determinations, 90 were elevated. In addition to the expected elevation in the myeloproliferative syndrome and patients with renal disease, five of 17 patients with metastatic carcinoma had significant elevations not associated with leukocyte abnormalities or renal disease. An additional 83 determinations showed that 13 out of 47 patients with carcinoma had significant elevations. The majority of the elevations were observed in patients with adenocarcinoma of the gastrointestinal tract. There appears to be no correlation with the stage, duration or therapy of the disease at this juncture.

MR041.20.01-0191

BLOOD PRESERVATION: INTEGRITY OF THE RED CELL MEMBRANES. R.A. Burningham. Naval Hospital, Philadelphia.

The experimental design was modified to investigate hemolytic mechanisms and coagulopathies in patients with hypertension. Screening studies consisting of a complete blood count, Coombs' test, prothrombin time (PT), non-activated partial thromboplastin time (NPTT), platelet count, Stypven clotting time, fibrinogen level, fibrin or fibrinogen-degradation products, were performed in patients admitted to the Medical Service with the diagnosis of hypertensive vascular disease.

All patients had diastolic blood pressures greater than 100 mmHg. Blood urea nitrogen and liver function studies were normal. There was no evidence of infection or underlying blood dyscrasia. Forty-six separate screening studies were performed on 40 patients. Seven patients were found to have a significant reticulocytosis without anemia. The red cell morphology was abnormal, but not specific. A definite hemolytic mechanism could not be established. One patient showed fibrin-degradation products on repeated assays, with an otherwise normal coagulation pattern.

MR041.20.01-0126

EXPERIMENTAL HEMATOMA IN GUINEA PIGS AND EFFECT ON SERUM HAPTOGLOBIN LEVELS. R.A. Burningham and J.E. Engeler, Jr. Naval Hospital, Philadelphia.

Low serum haptoglobin levels have been reported in patients with hematomas; however, correlation with extent, duration and mode of formation has not been established. This study will: investigate the effect of experimentally produced hematomas on serum haptoglobin levels under controlled conditions; determine the extent and duration of alteration of haptoglobin levels; and determine the amount of blood (in relation to total blood volume) needed to decrease haptoglobin level.

Initially, all seven guinea pigs were bled to 30% of the calculated blood volume, and hematoma formation was induced in the paraspinous muscle group. Haptoglobin levels were determined at 2, 8, 24, 72 and 144-hour intervals. Four of seven guinea pigs expired before the studies were completed. One guinea pig showed a slight drop in haptoglobin level and the remaining two showed no change. Appropriate controls were established.

This study is being continued using the rabbit, since the guinea pig proved unsatisfactory for technical reasons. In addition, hematomas will be induced in two sets of animals — one in which the hematoma is adjacent to a major blood vessel, and one in which the hematoma is not adjacent to a major blood vessel; all other conditions will remain constant.
CICC 3-05-124

EFFECT OF MALARIA OR PHYTOHEMAGGLUTININ (PHA-P) ON TRANSPLANTED L1210 MURINE LEUKEMIA. R.A. Burningham and C. Caldwell. Naval Hospital, Philadelphia.

This study is designed to determine the effect of stimulation of the immune system on survival rates in acute leukemia. Immunologic stimulation is achieved by inoculating DBA mice (leukemia induced by 7, 12-dimethylbenz [a] anthracene and related compounds) with *Plasmodium berghei*. The mice are then inoculated with L1210 leukemia, and along with suitable controls, survival is measured in each group. Each animal is examined post-mortem and the cause of death determined. To date four series of experiments have been performed. Preliminary results indicate that there is a statistically significant increase in survival of those animals receiving both malaria and leukemia when compared to appropriate controls.

It has been reported that PHA-P will also prolong survival in DBA mice inoculated with L1210 leukemia

by stimulation of the immune system. In order to substantiate these results a pilot study was set up utilizing three groups of five mice each, each receiving 10^5 L1210 leukemic cells. PHA-P was given either before or after leukemic implantation and the third group received normal saline as a control. The results from this small group of animals failed to confirm the initial report; there appeared to be some increase in survival in the group receiving PHA-P after leukemia implantation and no difference in the pretreatment group was observed. Further studies are now in progress.
CICC 2-05-610

ELECTRON MICROSCOPY STUDIES IN BLOOD DYSCRASIAS: A COLLABORATIVE STUDY. R.A. Burningham and C. Caldwell. Naval Hospital, Philadelphia.

Studies with the electron microscope (EM) have demonstrated structural variations between normal and leukemic blast cell forms. This project was designed to study further the ultrastructure of cells in leukemia, lymphoma, plasma cell dyscrasia, and preleukemic states. In collaboration with Dr. Harold Schumacher, tissue collected from 55 patients to date has been fixed in gluteraldehydeosmium solution and processed for examination with the Zeiss GS electron microscope. The material is currently being examined and analyzed. Of special interest is the finding by Dr. Schumacher of viral particles within the mitochondria of leukemic blast forms (Schumacher et al, *Blüt* 25: 169, 1972). Currently studies are underway to examine serially material acquired from patients with leukemia during pretreatment, reinduction, remission, and relapse phases. Viral particles, the association of these particles with mitochondria, and the extent of mitochondrial injury, if present, will be observed. In addition, studies will be undertaken to correlate the EM changes with DNA, RNA, and protein synthesis using radioisotope techniques (Schumacher et al, *Cancer* 18: 819, 1965). Tissue culture techniques combined with ultracentrifugation will be established for studies *in vitro*. Cellular components for viral particles, in association with specific cell structures, will be examined.
CICC 3-05-123

INDUCTION OF MURINE LEUKEMIA WITH HUMAN HEPATITIS SERUM. R.A. Burningham, M.A. Habib and M. Yoeli. Naval Hospital, Philadelphia and New York University, New York.

An acute lymphoid leukemia has been induced in A/J mice by the intraperitoneal injection of serum

from a human source. The leukemia has been successfully propagated through 23 passages with no change in virulence. In progress are electron microscopical studies, to determine the presence or absence of viral-like particles in the cells.

An initial set of neutralization studies comparing convalescent hepatitis associated antigen (HAA)-negative vs. HAA-positive sera showed significant prolongation of survival in mice given leukemic-cell suspension incubated with pooled, convalescent HAA-negative sera. Subsequent attempts to confirm those findings were unsuccessful. However, the most recent set of neutralizations, again, seems to indicate a protective effect of HAA-negative serum.

Further studies will include: (1) Rechallenge of survivors of previous neutralizations with known lethal doses of antigen, to see if immunity has been induced. (2) Challenge of mice given sublethal doses of antigen with lethal doses; also to determine if immunogenicity exists. (3) A time-course study of the disease, involving serial sacrifice of mice given lethal doses of antigen. Investigation of the transmissibility of this leukemia will be explored using cell-free solutions prepared by ultrasonic vibration and ultra-filtration (*Lancet* ii:1009, 1971), or differential centrifugation (*Brit J Haemat* 20: 587, 1971). Successful transmission by a subcellular fraction (or fractions) is important in establishing a possible viral etiology.

CICC 3-05-122

EOSINOPHILIA KINETICS AND FUNCTION IN HYPER-EOSINOPHILIA SYNDROMES. R.A. Burningham and D.N. Pasquale. Naval Hospital, Philadelphia.

This study is designed to measure the clearance of tagged eosinophils from the circulation, and to correlate the slope of the clearance rate with the presence or absence of symptoms attributable to histamine, 5-hydroxytryptamine, or bradykinin states of diverse etiology.

Delivery of a Nuclear Chicago Scintillation Counter is anticipated. Contact has been made with Dr. Eugene Cronkite, Brookhaven Research Institute, Long Island to visit his laboratory and review the technical aspects of tagging leukocytes for kinetic studies. Letters have been exchanged with the Commanding Officer, NAMRU No. 3, Cairo, Egypt to determine base line kinetic patterns on 10-15 human volunteers with hyper-eosinophilia secondary to chronic parasitism. Additional studies will then be performed on human volunteers at this hospital.

MR041.20.01-0393

IN VITRO BONE MARROW ORGAN CULTURES.

R.F. Granatir. Naval Hospital, San Diego.

Many drugs affect the bone marrow, directly or indirectly, by stimulation or depression of the hematopoietic elements. An *in vitro* system would afford an opportunity to study these effects and the site of action. We have developed such a system in which concomitant erythroid and myeloid precursors can be studied.

To date, we have demonstrated that these precursors can be stimulated to increase development and differentiation. Presently, we are studying the effect of marrow-suppressive drugs. In the future we hope to be able to predict the marrow reserve a patient will have before he undergoes chemotherapy.

CICC 3-16-128

DISORDERS OF HEMOGLOBIN SYNTHESIS IN NEWBORN FILIPINOS. H.M. Koenig, N.G. Tsoulos, S.A. Balch and J.E. Lang. Naval Hospital, San Diego.

The thalassemia syndromes and hemoglobin disease are quite common in the people of Southeast Asia and China. Alpha-thalassemia is prevalent throughout this area of the world, and its homozygous form is incompatible with life. All newborn Filipinos born at this hospital now receive a cellulose-acetate electrophoresis determination using their cord blood.

So far, approximately 100 infants have been studied. Three infants have had detectable amounts of Hemoglobin Barts (Hgb 4) in their cord blood. One of these infants has been followed for five months and presents the clinical expression of the alpha-thalassemia trait. Techniques for quantifying Hemoglobin Barts have been elucidated using starch-block electrophoresis.

Subsequent to discovery of infants with detectable levels of Hgb Barts, we hope to measure ratios of synthesis of various globin chains in their peripheral blood. Techniques of carboxy-methylcellulose chromatography of radioisotope-labeled globin chains are presently being determined. In identifying the abnormal hemoglobin patterns in Filipino infants, we hope to determine: (1) the incidence of the hetero and homozygous forms of alpha-thalassemia in the Filipino, (2) the cause of fetal wastage in many stillborn Filipinos, and (3) means to enhance the understanding of the inheritance of the genes controlling alpha-chain synthesis.

CICC 3-16-039

FACTOR VIII LEVELS IN MENORRHAGIA. J.E. Kostinas. Naval Hospital, Portsmouth, Va.

Von Willebrand's disease in the female may be manifested as recurrent unexplained menorrhagia. A study is underway utilizing Factor VIII levels as a screening procedure. Since the incidence rate of von Willebrand's disease in a given population is unknown, a large sample of patients presenting to this facility with unexplained menorrhagia will be screened. Low Factor VIII levels will be confirmed by repeat examination and those patients having two levels below 60% will be further evaluated historically and with a complete bleeding survey.

If the incidence of von Willebrand's disease is high in patients with menorrhagia, it is possible that they may segregate into a group which can be more easily identified than at present. This segregation would be of considerable interest to the gynecologist in the management of these patients. In addition, an incidence figure for a selected population (female, menstruating) would be established.

Sixty-one patients with unexplained menorrhagia have been studied to date, and the preliminary data are not significant.

CICC 2-08-510

DEFIBRATION SYNDROME IN HYPOTENSIVE AND SEPTIC STATES RELATED TO COMBAT MEDICINE. J.E. Lang. Naval Hospital, San Diego.

The clinical entity of disseminated intravascular coagulation (DIC) is known to occur in many settings. During the past year patients with different problems were studied as models of DIC; their problems included meningococcal disease, fat emboli, preeclampsia-eclampsia, effects of certain anesthetic gases, chronic hepatitis, autotransfusing coronary bypass procedures and miscellaneous situations. All of these entities have been studied during the past year.

Computer analysis of the data on meningococcal patients indicated that Factor V and platelet count (less than 50% and 100,000 mm³, respectively), on the initial study, is significant statistically; these patients will develop clinical DIC. Long-bone fractures associated with the fat embolus syndrome demonstrated varying results in coagulation studies; no definite pattern could be elucidated. Preeclamptic and eclamptic patients demonstrated DIC changes only in the eclamptic state. The Bently autotransfuser, in primates and man demonstrated marked DIC and further investigation is underway. Recent evidence for DIC, in certain patients with chronic acute hepatitis, has been found and is

being studied. The effect of anesthetic gases on the coagulation mechanism is being evaluated at this time.
M4305.05-3033

DELIVERY OF HEALTH CARE: A PERSPECTIVE STUDY FOR EVALUATION OF ANEMIA IN MILITARY MEDICINE. J.E. Lang, S. Armstrong and R. Donnell. Naval Hospital, San Diego.

This study was initially developed to be an integral part of the RDT&E Automated Multiphasic Screening Program; however, the latter was deferred for later implementation. As an alternative, a detailed appraisal of both inpatient and outpatient consultations to the Hematology Branch have been evaluated for the period 1 Jul 1972-1 Dec 1972 in order to establish trends. Of the 192 consults reviewed, 56 patients (28 inpatients and 28 outpatients) were referred for evaluation of "anemia." The remainder required consultation for white blood cell, platelet and lymphocyte disease, and coagulopathies. In this setting, it became readily apparent that the results are distorted because the referring physician frequently instituted iron therapy, thereby excluding "iron deficiency" as a category in our group. "Secondary" anemias and anemia associated with other hematologic disease were the most frequently defined categories, with the former predominating. Using other terminology, the "hypoproliferative" group appears to be emerging as the larger; however, more sampling is required, and the need for initial exposure to the patients (i.e., multiphasic screening procedures) would greatly benefit the study.

CICC 3-16-156

COMPLEMENT RECEPTORS ON HUMAN LEUKEMIC LEUKOCYTES. G.L. Logue and J.F. Bubinak. National Naval Medical Center, Bethesda.

The purpose of this study is to determine if receptors for activated human third component of complement (C3) are present on leukocytes of patients with various leukemic disorders. Activated C3 is added to human red cells by cold reactive (Anti I) antibodies. Adherence of these C3-coated cells to leukemic leukocytes is determined by microscopic examination for rosette formation and by attachment of the leukocytes to glass wool columns.

Preliminary studies of leukocytes from patients with chronic granulocytic leukemia have shown complement receptors to be present. Leukocytes from one patient with acute granulocytic leukemia also had these receptors. The presence of these receptors will be related to the abnormalities of immune globulins in patients with

lymphatic leukemia. These studies are still in preliminary phases and further data must be collected before any conclusions may be reached.
CICC 3-06-191

PATHOGENESIS OF ENDOTOXIN SHOCK IN MILITARY MEDICINE. W.E. Lucas and J.L. Kitzmiller. Naval Hospital, San Diego.

The roles of disseminated intravascular coagulation and complement-dependent immune reactions in the pathogenesis of animal endotoxin shock have been examined.

Endotoxin in two dosage levels was administered to normal cats and cats pre-defibrinogenated with the fibrinogen-converting factor of Malayan pit-viper venom, to test the role of intravascular coagulation in the production of endotoxin shock. There were no significant differences in survival, hemodynamic responses, hematologic as well as chemical parameters, or pathologic findings between the two groups of cats.
MR041.20.01-0351

LEUKOCYTE STUDIES USING THE CELL SEPARATOR. C. Strife and E. Perlin. Naval Hospital, NMMC, Bethesda.

The continuous flow blood cell separator is being used for several studies concerning human peripheral leukocytes. In order to determine the most efficient method of collecting granulocytes for clinical transfusion, the cell separator is being compared with the nylon-wool filter. Because of several episodes of severe bradycardia which occurred in normal donors during leukocyte collections with the nylon-wool filter, the clinical use of these filters has been suspended.

An effort has been made to determine the most effective way of removing leukocyte antigens from whole blood. Several methods, including continuous washing-centrifugation in the cell separator have been tested. The lowest quantity of residual leukocyte antigens is found when the red cells are frozen and thawed prior to saline washing.

Another facet of this study is whether delayed hypersensitivity to specific antigens can be transferred passively through the infusion of allogeneic peripheral lymphocytes. It is too early to draw definite conclusions about this.

CICC 3-06-169

CLOTTING STUDIES AND PLATELET FUNCTION IN PATIENTS WITH CARDIAC PROSTHESES. J.W. Weaver, A.D. Hagan and J.E. Lang. Naval Hospital, San Diego.

Clotting factors and platelet function are of special importance in the patient who has developed variant function of his prosthetic valve. Considering the life-threatening consequences of either not detecting ball variance, or submitting patients with suspected ball variance to unnecessary open heart surgery, it is obvious that additional noninvasive methods to detect ball variance are needed.

Patients will be selected from those with prosthetic valves presently being followed by the Cardiology-Thoracic Surgery Clinic. Specifically, the following base-line blood studies will be determined: platelet survival time, platelet aggregation studies, a complete clotting battery, and phonocardiograms. These tests will be examined as they become available.

To date, progress has consisted of a literature search for background and related information and three candidates have been studied in all areas other than platelet half-life. License to use radioisotopes is still pending but expected momentarily. A quantity of patients, selected from the Cardiology and Thoracic Surgery Services is available now for study.

CICC 3-16-048

IMMUNOLOGY

SUPPRESSION OF DELAYED HYPERSENSITIVITY IN ACUTE VIRAL HEPATITIS. L.A. Bucklew and J.B. Smith. Naval Hospital, Bethesda.

Eighteen patients with acute viral hepatitis (AVH) were tested for delayed hypersensitivity (DH) to six common skin-test antigens during the acute phase of their hepatitis and after complete convalescence.

Twelve patients (Group A) were anergic to all skin test antigens during the acute phase of their hepatitis, with return of DH reactions after convalescence. Five patients (Group B) were not anergic during acute hepatitis and had no significant change in their DH reactivity after convalescence. One patient was anergic both during the acute illness and after convalescence, and was lost to follow-up.

The incidence of anergy in this group of patients with AVH (13/18) was significantly higher than in a group of age- and sex-matched controls (2/22) ($p < 0.001$). Patients in Group A (anergic during the acute

phase of their hepatitis) tended to have a more prolonged illness than those in Group B.
CICC 2-06-312

E.S.R. MEASUREMENTS ON HUMAN TISSUES AS A CANCER INDICATOR. E.D. Finch and D.K. Heffner.

Naval Hospital and Naval Medical Research Institute, NNMC, Bethesda.

The purpose of this study is to explore the possibility of using electron spin resonance (e.s.r.) as an indicator of malignant disease. The first human tissues examined gave results which were disappointing in that they appeared nonspecific. However, a concomitant series of experiments on animal tissues gave unexpected results. A group of control animals which had been injected with typhoid vaccine gave reproducible e.s.r. signal changes very early in the time course of the immune response. This project involving human tissues is terminated pending the further study of this immune phenomenon by appropriate animal studies. If warranted by the animal studies, further investigation on human tissues may be done in the future.
CICC 2-06-308

BIOCHEMISTRY OF THE ALTERNATE (PROPERDIN) COMPLEMENT PATHWAY AND RELATION TO INFECTIOUS SHOCK. L.G. Hunsicker. Naval Hospital, Portsmouth, Va.

Recent work indicates the existence of a mechanism for the activation of the complement system distinct from the classical early complement components, and apparently identical to the properdin system of Pillemer. Several recent studies suggest a role for the properdin system in initiation of coagulation, and possibly of the kinin-forming and fibrinolytic systems. The facts that the properdin system is easily activated by endotoxin, that the system is involved in defense against bacterial sepsis, and that the coagulation and other pathways apparently activated by the properdin system are involved in the pathogenesis of infectious shock, all suggest that the properdin system may play a central role in the infectious-shock syndrome.

The present study is intended to extend previous investigations of the biochemistry and normal physiology of the properdin system, and to study, *in vitro* and *in vivo* its contribution to the infectious-shock syndrome.
M4305.05-3090

ROLE OF THE ALTERNATE (PROPERDIN) COMPLEMENT PATHWAY IN HUMAN DISEASE. L.G. Hunsicker. Naval Hospital, Portsmouth, Va.

The role of the complement system as a mediator of humoral immune responses has been appreciated in several human diseases, including glomerulonephritis and lupus erythematosus. It has been demonstrated recently that an alternate mechanism for activating the complement system exists, and appears to be identical to the properdin system described by Pillemer. Considerable evidence exists in the older literature that the properdin system is of major importance in host defense against bacteria. More recent evidence implicates the properdin system in glomerulonephritis and lupus.

The present work undertakes to extend previous studies of the biochemistry of the alternate (properdin) complement pathway, and to study its role in disease. Measurements of component levels and immunofluorescent microscopy of pathologic material, from patients with those diseases appearing to involve this system, are planned.
CICC 3-08-180

TEST OF IMMUNOGENICITY OF POLYMERS OF AMINO ACIDS IN MAN AND THE RELATIONSHIP OF HISTOCOMPATIBILITY TYPE. I. Scher and I. Green. National Naval Medical Center, Bethesda.

The immune response to an antigen and the susceptibility to immune-mediated diseases in experimental animals has been closely related to their histocompatibility type. The recent demonstration of an association of HL-A type and certain human diseases may indicate a possible relationship between histocompatibility type and immune responsiveness in man. In order to study this relationship, the synthetic polypeptide antigen Glutamic Acid-Lysine-Tyrosine (GLT) is being used to immunize human volunteers. Immune responsiveness to this antigen is being determined by antibody determination, delayed hypersensitivity and *in vitro* lymphocyte stimulation. Each volunteer is HL-A typed.

Preliminary data indicate marked variations in the ability to develop immune responsiveness to the GLT. The small numbers of volunteers tested do not allow correlations to be made with HL-A type at this time.
CICC 3-06-132

INFECTIOUS DISEASE

CLINICAL AND LABORATORY EVALUATION OF DIAGNOSTIC TESTS FOR NEISSERIA GONORRHOEAE. F.S. Billingsley and D. Martin. Naval Hospital, Bethesda.

The purpose of this study is to determine the incidence of *Neisseria gonorrhoeae* infection at the Bethesda Naval Hospital and to compare the reliability and accuracy of the Organon Agglutination Technique with standard laboratory methods. Due to the magnitude of the current VD epidemic in this country, it has been recommended that routine screening for gonorrhea be performed. Organon has developed a rapid serologic test, and its reliability is being determined.

All obstetrical and gynecological outpatients, 35 years of age and under, will be simultaneously screened by serologic and culture testing.
CICC 3-06-168

HOST DEFENSE MECHANISMS IN ACUTE MENINGOCOCCEMIA. M.S. Erdos, J.E. Lang and E.A. Edwards. Naval Hospital, San Diego.

This study will evaluate the effectiveness of the host defense mechanism in patients with acute meningococcal infections. This part of the study will determine if these patients have suppressed function of their white blood cells or immune system. We plan to assess the role that the concentration of meningococci and the breakdown products of their cell walls, in the blood and spinal fluid play in the production of disease by this organism. Ultimately, we hope to apply information obtained in this study, to determine specific methods of treating patients with fulminant clinical disease caused by the meningococcal organism.
MR041.20.01-0385

NITROBLUE TETRAZOLIUM TEST. P.J. Kovalcik. Naval Hospital Boston, Chelsea.

The nitroblue tetrazolium (NBT) test is being performed to aid in the diagnosis of postoperative fever. This test is based on the increased spontaneous reduction of pale yellow NBT dye to blue-black crystals by peripheral blood neutrophils in the presence of bacterial infection.

Since the study began in Jan 1972, ten patients undergoing major upper abdominal surgery at the Naval Hospital Boston have been studied, both preoperatively

and for several days postoperatively. This test is feasible and offers promise in the evaluation of postoperative fever.

CICC 2-02-107

NEOPLASTIC DISEASE

⁶⁷GALLIUM SCANS IN THE STAGING OF MALIGNANT DISEASES. E.M. Braun and T.J. Lapine. Naval Hospital Boston, Chelsea.

The concentration of the exogenously-administered radioisotope ⁶⁷gallium is increased in malignant tissue as compared to normal tissue. In this study, whole-body scans are performed 72 hours after isotope administration to patients representing a wide variety of malignant disease. The results of the gallium scan have been correlated with other available clinical parameters to evaluate the usefulness of the scan as a staging device.

To date, we have performed 56 gallium scans, most involving patients with lung or breast cancer, or lymphomas. Overall, we have found that positive scans are obtained in most cases of bronchogenic carcinoma, and may sometimes be of great value in determining the extent of disease. In breast cancer, the gallium scan is usually quite accurate in identifying sites of metastasis in disseminated cases, but has not proven reliable in distinguishing benign from malignant primary breast lesions. Lymphomas have a high incidence of positive scans but other methods seem to be more valuable in identifying paraortic nodes and splenic involvement. In miscellaneous tumors as well, the gallium scan is often a helpful staging procedure in that it may identify sites of disease that have otherwise been undetected.
CICC 2-02-111

CLINICAL CANCER RESEARCH. E.M. Braun. Naval Hospital Boston, Chelsea.

Patients with advanced cancer are treated, when appropriate studies are available, under drug treatment protocols of the Eastern Cooperative Oncology Group. At the present time, 18 protocols are being utilized by this group, in pharmacological and toxicological studies, clinical trials, and comparative studies.

Since 1 Jul 1972, eleven patients from this hospital have been entered into such studies. A wide range of malignant diseases is represented. When combined with similar patients from other institutions and analyzed, the therapeutic modality under investigation

may be evaluated in a statistically significant manner and within a relatively short period of time. By entering suitable patients into protocol studies, an important contribution is made to the total effort of clinical cancer research.

CICC 3-02-081

NAVY COOPERATIVE CHEMOTHERAPY GROUP.

R.A. Burningham, J.E. Kostinas, R. Moquin, G. Lang and C. Kardinal. Naval Hospitals; Philadelphia, Portsmouth, Bethesda, San Diego, and Oakland.

Two protocols have been submitted to the National Cancer Institute and approved for study by the Group. The first protocol is Navy Cooperative Oncology Group (NCOG) No. 7201: "Treatment of Advanced or Refractive Acute Myeloblastic Leukemia." This study uses a combination of hydroxyurea (NSC No. 32065), 6-mercaptopurine (NSC No. 755), and dexamethasone (NSC No. 34521). To date three patients have been entered into study. One patient had no response, the second patient had a partial response, and the third patient remains on study. It is anticipated a total of 20 patients will be placed on study during the next 12-18 months.

The second protocol, NCOG No. 7202: "The Use of Emetine Hydrochloride (NSC No. 33669) In Enteric Adenocarcinomas," has been recently activated and two patients are currently on study. It is anticipated 25 patients will be entered into this study in the next 12 months.

For the next year the major activity of the Group will lie in disease-oriented Phase II studies, and each principal investigator has been asked to develop at least one protocol in this area of investigation. More frequent meetings have been urged by the Group in order to exchange ideas and develop these studies.

CICC 2-05-609

CHEMOTHERAPY OF SELECTED BLOOD DIS-

EASES. R.A. Burningham, C. Caldwell and A. Suvari. Naval Hospital, Philadelphia.

The Hematology and Medical Oncology Branches, Internal Medicine Service have had membership in the Acute Leukemia Group B (ALGB) cooperative chemotherapy group since 1967, and in the Eastern Cooperative Oncology Group (ECOG) since 1970. The essential goal of these groups is to systematically place, initiate, execute, evaluate, analyze, and report on research methods of diagnosis and treatment of patients with neoplastic diseases.

A total of 139 patients have been entered into ALGB protocols and 33 patients into ECOG protocols.

During 1972, 53 patients were entered into study.

Sixty patients continue on study at the present time. Diagnosis distribution for 1972 is as follows: Carcinoma-25, malignant lymphomas-19, multiple myeloma-2, chronic leukemias-2, acute leukemias-5. A number of other patients have been entered into pilot studies.

It is anticipated that the majority of patients who come under the responsibility of the Hematology and Medical Oncology Branches will be entered into these studies, thereby making significant contributions to patient care and training programs. Since this Naval Hospital is actively engaged in the large cooperative endeavor, greater efforts will be made to increase patient referral for evaluation and incorporation into these studies. Every attempt will be made to return patients to their referring physicians for continued treatment and follow-up. As a result of these efforts a multidisciplinary approach to the cancer patient is being developed and plans are underway to establish an Oncology Service here.

CICC 3-05-152

CHEMOTHERAPEUTIC AGENTS IN THE TREATMENT OF LUNG TUMORS. **M.J. O'Sullivan, Jr., and R.G. Fosburg.** Naval Hospital, San Diego.

During the past year, in association with the National Cancer Institute, a chemotherapeutic agent CCNU, a nitrosourea compound, has been used in the treatment of advanced carcinoma of the lung. The results have been promising and a further extension of its use is proposed.

Twenty-five patients with the diagnosis of carcinoma of the lung, despite the stage of the disease, were considered for therapy. Thus, several patients with end-stage disease were accepted for therapy. No beneficial results were noted in this class of patients. Thirteen patients have died (twelve of their disease and one a suicide). Two patients have been declared failures of therapy and were submitted to X-ray treatment. One patient developed superior vena cava syndrome while under treatment; the other patient, with a huge localized chest-wall tumor, showed no clinical response after several courses of treatment. In the remaining patients: there has been one complete remission (oat cell carcinoma, alive one year post-diagnosis and clinically free of disease); there have been several partial remissions, and others in whom symptoms of metastatic lesions have been palliated. The drug has shown promise in the treatment of lung carcinoma and its use will be continued.

CICC 2-16-405

PLATELET FUNCTION IN LYMPHOMA AND SOLID-TUMOR PATIENTS, PRIOR TO, DURING, AND AFTER THERAPY. D.N. Pasquale, C. Caldwell and A. Suvvari. Naval Hospital, Philadelphia.

The purpose of this study was to determine the presence of platelet function abnormalities in patients with neoplastic diseases, especially lymphomas and solid tumors, prior to therapy and during the course of the disease.

To date the platelet factor 3 release test and the platelet aggregation studies using the Chrono-log aggregometer have been standardized using normal volunteers. In addition to the normal controls five patients with cancer have been studied. All had received no prior therapy, except for one patient who received local X-ray treatment. There has been no difference between the normal controls and the patients studied. Platelet survival assessment was not performed since the scintillation counter has not been installed to date.

The projected plan is to study a minimum of 30 patients. If a definite pattern is found, as has been noted in patients with acute leukemia, the study will be extended to include more patients.

CICC 3-05-125

USE OF DAUNORUBICIN & L-ASPARAGINASE IN PATIENTS WITH ACUTE LEUKEMIA. E. Perlin; J.W. Reid, Jr.; J. Logue; and R.B. Moquin. Naval Hospital, Bethesda.

We have treated 16 patients (pts) with acute leukemia (AL) using the investigational chemotherapeutic drugs, daunorubicin (DNR) and L-asparaginase (L-ASP). The regimens were as follows: (1) DNR 30-40 mg/m² days 1&2; cytarabine (Ara-C) 100 mg/m² days 1-5; methylprednisolone 500 mg/m² days 1-5, and vincristine 2.0 mg day 1; (2) L-ASP 200 I.U./kg daily until remission. The results were as follows: 13 pts with AL of adults were given (1); 7/13 had a complete response (CR) (5% blasts in bone marrow); 2/13 had a partial response (PR) for a total R of 69%. All responders but one had acute myelocytic leukemia (AML). The longest survivor thus far lived two years. Five pts with acute lymphatic leukemia were treated with L-ASP: one had an allergic reaction to *E. coli* preparation, but tolerated the *Erwinia* preparation; 3/5 had a CR.

DNR & L-ASP are effective agents for AL. They were generally well tolerated with no serious acute toxicity. Collection of data is continuing.

CICC 2-06-348

USE OF NITROSOUREA COMPOUNDS IN MALIGNANT DISEASE. E. Perlin; J.W. Reid, Jr.; J. Logue; and R.B. Moquin. Naval Hospital, Bethesda.

The nitrosourea compounds are new chemotherapeutic agents undergoing clinical trials in patients with cancer (Ca).

We have treated 19 patients (pts) with BCNU (bis chloroethyl-nitrosourea) and 22 pts with CCNU (1-[2-chloroethyl]-nitrosourea). The results in the BCNU group were: 2/5 pts with Hodgkin's disease (HD) had a partial response (PR). 1/4 pts with Ca of the stomach had a PR and lived almost three years post-diagnosis (drug given with 5-fluorouracil). 1/2 pts with glioblastoma multiforme and 2/2 pts with myeloma had a PR. 0/4 pts with melanoma, 0/1 with oat cell Ca of the lung and 0/1 with terato-Ca of the ovary responded.

Of the CCNU group, 15 pts with Ca of the lung failed to respond; one has had stable disease. 1/2 pts with astrocytoma appeared to respond, as did 1/2 with HD. 0/1 hepatoma, 0/1 pancreatic Ca and 0/2 colon Ca responded. Tolerable toxicity included nausea, vomiting, and bone marrow depression 21-35 days after drug initiation; 4 pts who had received CCNU & 3 pts who had received BCNU had moderately severe thrombocytopenia; all had received other chemotherapy.

The nitrosourea compounds appear to be useful in HD, myeloma, and brain tumors; they appear to have limited usefulness in lung Ca. Their use in other solid tumors is still under study.

CICC 2-06-304

USE OF BLEOMYCIN IN THE TREATMENT OF MALIGNANT DISEASE. E. Perlin; J.W. Reid, Jr.; and J. Logue. Naval Hospital, Bethesda.

The bleomycin preparation (Bleo) is a mixture of antibiotic polypeptides isolated from *Streptomyces verticillus*. Bleo has been reported to be useful in Hodgkin's disease (HD), head and neck cancer (H&N), and in testicular tumors. Reported toxic effect of the drug is fibrosis of the skin and lungs.

We have treated nine patients (pts) with this drug. Six pts received Bleo alone. Our data show: 3/3 pts with H&N had no change (NC = stable course); 0/2 pts with HD had no response (NR = progressive course); and 2/2 pts with testicular cancer, who received Bleo alone, had NC. In 2 pts the drug was given in combination: One pt with testicular cancer, who received vinblastine and Bleo had a complete response (CR); One pt with HD, who received vincristine, prednisone and Bleo had a good partial response (PR). Four pts

developed fibrotic nodules on their fingers; one had stomatitis. None had pulmonary fibrosis.

The drug may have special value in pts with depressed bone marrow, since it is relatively less toxic to hematopoietic cells than other chemotherapeutic agents.

CICC 2-06-348

NEUROLOGY

CEREBRAL AND SUPRASEGMENTAL DETERMINANTS OF MUSCLE CELL DIFFERENTIATION. H.

Travers. Naval Hospital, Portsmouth, Va.

Recent research into skeletal muscle development has led to the concept of motor unit uniformity where muscle cells differentiate biochemically and morphologically in a manner specific to the type of motor neuron which innervates them. Those factors important in the differentiation of type-specific lower motor neurons have yet to be completely elucidated. There is some evidence that suprasegmental structures may influence the maturation of the motor unit.

In order to clarify the developmental effects of upper motor neurons on lower motor neurons and, ultimately, muscle cells early in embryonic life, Wistar rat fetuses were subjected to intra-uterine decapitation on the 16th day of gestation. At-term fetuses were taken by cesarean section; the normal and decapitated animals were sacrificed and the hind legs were sectioned at comparable levels and stained histochemically for adenosine triphosphatase, phosphorylase, and succinic dehydrogenase — techniques which separate muscle cells into two distinct types of muscle fibers.

Comparison of tissue taken from normal and decapitated fetuses indicates that the upper motor neuron plays no role in motor unit cytodifferentiation.

CICC 2-08-515

NEUROSURGERY

MICROSURGERY: ITS APPLICATION IN NEUROSURGERY, VASCULAR SURGERY AND PLASTIC SURGERY. M.A. Caccac and A.F. Figueroa. Naval Hospital Boston, Chelsea.

A new operating room microscope and a new bipolar coagulator for use in microsurgery have been acquired. Some microsurgical instruments and suture

material have also been acquired to supplement personal equipment belonging to the investigators. Since April 1972, General Surgery residents, rotating in Neurosurgery for two months, have been tutored by the principal investigator in the proper way to use an operating room microscope and micro-instruments. Practice sessions were held using cadaver vessels before attempts were made on laboratory animals. Once a week, various microvascular techniques were practiced on rabbits, i.e., longitudinal incision and closure, end-to-end anastomosis and end-to-side anastomosis, on the femoral arteries. This helped to refine and perfect the techniques of microsurgery in preparation for actual operating room experiences.

In the operating room, the investigators have used the operating room microscope successfully in performing total removal of cerebellopontine-angle tumors without sacrificing the facial nerve, in total removal of arteriovenous malformations in the brain, in intramedullary tumors, and in cerebral aneurysm surgery. A total removal of an inoperable calcified craniopharyngioma was also done using the trans-callosal approach, completely dissecting the tumor from the brain stem and the basilar artery.

CICC 2-02-119

TRANSVENTRICULAR HYPOPHYSECTOMY. C.B.

Early and J. Sode. Naval Hospital, Bethesda.

A method of pituitary ablation, significantly more simple than any other method presently available, is being developed. A Seldinger wire is passed through a small twist-drill opening in the frontal skull, and guided under fluoroscopic control into the cerebral lateral ventricle, thence through the foramen of Monro and the third ventricle, down the infundibular recess and pituitary stalk into the hypophysis of a monkey. The wire is electrically insulated, except for its tip embedded in the hypophysis. Radiofrequency electrical current is then passed through the wire to effect pituitary ablation.

The efficacy of the ablation procedure is evaluated by assessing the degree to which pituitary function is eradicated, as determined by endocrine analyses. To date, an insufficient number of procedures have been performed to permit a forceful statement regarding the efficacy of the method. However, the adequacy of the lesion as assessed by early post-mortem examination has been demonstrated. Further, proper placement of the wire in the hypophysis in the live animal has been effected. It appears probable that documentation of

the efficacy of the method will be provided by additional procedures.
CICC 2-06-333

DIAGNOSIS AND TREATMENT OF VASCULAR DISEASE IN NAVAL PERSONNEL. W. Gee. Naval Hospital, Oakland.

To provide improved monitoring of cerebral blood flow in the casualty undergoing operation for carotid artery injury or brain trauma, it is planned to evaluate the effectiveness of ocular plethysmography.

A total of 15 clinical cases have been studied with excellent correlation with angiographic findings. When the intracranial pressure transducer is available, ocular pulse waves with variations in intracranial pressure will be studied.

MR041.20.01-0262

EFFECTS OF LYOPHILIZED ALLOGRAFT BONE ON REHABILITATION OF MILITARY PERSONNEL WITH INTERBODY SPINAL FUSIONS. G.F. Martin and L. Wrobel. Naval Hospital, San Diego.

Spinal degenerative disc disease imposes severe disability and loss of time on a significant number of active duty Fleet personnel. Conventional bone-grafting techniques employ autograft iliac-crest bone, thus increasing operating-room time, postoperative morbidity and rehabilitation time. It is anticipated that hospitalization can be shortened by as much as a factor of two, through the use of lyophilized allograft cancellous bone plugs for spinal-interbody fusion.

Active-duty patients entering Naval Hospital, San Diego with spinal degenerative disc disease will undergo conventional diagnostic examinations such as electromyograms and myelography. Candidates for operation will be selected on the basis of objective examination findings. Postoperative pain and rehabilitation time will be compared for groups of patients receiving autograft bone and lyophilized allograft bone. Specialized postoperative examinations of neck function will be obtained on video tape. These results will be compared with those documented for other groups of similar patients, through the Navy Tissue Bank-Graft Registry, in the hope of developing a superior method of rehabilitating active duty Naval personnel with degenerative disc disease.

Twenty-eight patients have undergone surgery. We are currently duplicating X-ray studies and preparing for presentation of the results as the patients report for their follow-up. Preliminary results convince this investigator that freeze-dried bone achieves a fusion

rate equal to that of autogenous bone. Follow-up exam will be conducted in two years.
M4305.03.3020

PERCUTANEOUS CERVICAL CORDOTOMY. J.B. Oldershaw. Naval Hospital, Great Lakes.

The Grass physiological SP stimulator and amphenol connector was obtained, tested and standardized. The Radionics Radiofrequency lesion generator was standardized, by producing lesions in brain slices in normal saline. These were found to approximate, on cut section, the lesions produced by Dr. Sean Mullan as previously described.

Several patients who were evaluated as candidates for this procedure were not used because of other risks — widespread disease in two cases, terminal state in one, and marked respiratory impairment in another.
CICC 2-13-020

TREATMENT OF ACUTE HEAD TRAUMA: INTRACRANIAL VASOSPASM. B.L. Rish. Naval Hospital, Bethesda.

The tolerance and efficacy of alpha-adrenergic blocking drugs will be evaluated in the treatment of intracranial vasospasm induced by subarachnoid hemorrhage. By placing a Silastic reservoir/catheter implant in the cisterna magna of the experimental animal, the spasm can be induced and treated via the same route, while detailed analysis is obtained by fluoroscopy, angiography and flow studies.

MR041.20.01-0332

OBSTETRICS-GYNECOLOGY

EVALUATION OF A TWO MINUTE SLIDE TEST FOR PREGNANCY USING HCG-COATED LATEX SUSPENSION, DRIED. R.L. Baker and J.C. Shaffer. Naval Hospital, Portsmouth, Va.

The PREGNOSTICON DRI-DOT Test for the detection of human chorionic gonadotropin (HCG) excreted in urine during pregnancy is based on the antigen-antibody reaction.

The above-mentioned test was performed on 1,181 women known to be pregnant, randomly selected from the Portsmouth Naval Hospital Obstetric Clinic; and on 602 women suspected of being pregnant, selected for that reason from the Gynecology Clinic of the same institution. Of 602 tests performed on specimens

received from the Gynecology Clinic, from women whose follow-up examination indicated pregnancy (documented by presence of fetal heart tones heard later in Obstetric Clinic), 229 had been tested prior to 50 days from the first day of the last menstrual period (FDLMP). This represents approximately 20% of the input into the overall obstetric load for the three-month period, as calculated from total deliveries.

In summary, the PREGNOSTICON DRI-DOT (PD-D) test for pregnancy was found to be reliable and sensitive. Its ease of use by even nonmedical persons seemed to be its most unique and desirable quality. It became apparent that by using a single technician, both reliability and sensitivity of all tests performed could be improved. The ease of use and inherent portability made the PD-D very useful for the resident covering emergency calls at night when other pregnancy tests were unobtainable. Enhanced efficiency in case management resulted.

CICC 2-08-509

POSTPARTUM CHEST X-RAY STUDIES OF 1,000 PATIENTS TO DETERMINE INCIDENCE OF PNEUMOPERICARDIUM AND PNEUMOMEDIASTINUM.

R.L. Baker and J.A. Sebastian. Naval Hospital, Portsmouth, Va.

Two cases of postpartum pneumopericardium without associated pneumomediastinum discovered at the Naval Hospital, Pensacola were studied. Routine X-ray examination of the chest was performed on 1,000 random postpartum patients at the Naval Hospital, Portsmouth, Va., and no evidence of pneumopericardium or pneumomediastinum was detected. Data from this study have been prepared for publication, and the literature on pneumopericardium and pneumomediastinum associated with pregnancy has been reviewed.

CICC 2-08-517

VAGINAL CUFF INFECTIONS. **S. Barchet, M. Birnbaum, D. Hanson and J. Porter.** Naval Hospital Boston, Chelsea.

Vaginal cuff infections following elective hysterectomy occur with such regularity and significant resultant morbidity to cause inordinately high costs in morbidity and economy of patient care. The problem is ill-defined and though prophylactic antibiotics are of great value in reducing both patient and economic costs, the use of prophylactic antibiotics could represent acceptable medical care if the source of microbiologic wound entry could be defined. The microbiologic data being accumulated from successive

hysterectomy specimens suggests that the use of pre-operative antibiotics as a therapeutic measure may well be justified.

CICC 3-02-063

PATHOPHYSIOLOGIC ADAPTATIONS IN PREGNANCY. **S. Barchet, M. Birnbaum, A. Munson, D. Hanson and C.R. Valeri.** Naval Hospital Boston, Chelsea.

Maternal-fetal red blood cell (RBC) functions, oxygen transfer mechanisms and dysfunctional uterine contractions are imperfectly understood despite recent advances in bioelectronic and laboratory technology. An improved understanding will better define normal and abnormal oxygen-transport relationships and aberrant labor patterns.

Multiple and serial determinations of biochemical phenomena, known to be related as mediators of RBC functions are being made. Fetal heart rate and intra-uterine pressure patterns are being collected, recorded and collated. Data accumulated from these studies and subjected to collation and interpretation, may provide improved definition of the elements producing and resulting in intrapartum asphyxia and hypoxemia. Such definition is mandatory to provide for intelligent management of complications affecting the maternal-fetal unit.

CICC 3-02-061

ELECTROENCEPHALOGRAM (EEG) CHANGES IN PATIENTS ON ORAL CONTRACEPTIVES. **F.S. Billingsley and W.L. Brannon.** Naval Hospital, Bethesda.

The purpose of this study is to determine if oral contraceptives cause any abnormal electrical activity in the brain and if changes do occur, are they readily reversible? Increasing reports of neurological disease associated with oral contraceptive medication have been reported, but a causal relationship has not been established.

In this study, base line EEGs and neurological exams will be obtained prior to initiating oral contraceptive therapy. No subjects will be chosen who have manifested any evidence of neurologic or gynecologic disease. Monthly studies will include EEG, blood glucose, blood urea nitrogen and electrolytes, cortisol, renin and thyroxine studies. To date the study group has been small and no definite conclusions can be drawn.

CICC 3-06-167

THE EFFECT OF ESTROGEN THERAPY ON PARAMETERS OF THYROID FUNCTION IN POSTMENOPAUSAL WOMEN. M. Birnbaum and T. Lapine. Naval Hospital Boston, Chelsea.

While it is known that estrogen in pharmacologic doses raises the serum thyroxine (T4) level by raising the serum level of thyroxine-binding globulin (TBG), it has not been established whether estrogen replacement therapy has the same effect.

Postmenopausal or ovariectomized women attending the GYN Clinic at Naval Hospital Boston have been selected for study. Those not receiving estrogen will serve as controls for those on the medication. Blood has been drawn from the study patients. Serum levels of T4 and TBG will be determined and the results analyzed to ascertain if there have been any effects resulting from the estrogen therapy.

CICC 3-02-075

RELATIONSHIP OF GESTATIONAL SERUM HEXOSAMINIDASE B LEVELS IN PATIENTS WITH EXCESS WEIGHT GAIN AND TOXEMIA OF PREGNANCY. R.C. Cefalo, R.S. Juskevich and J. Du Bois. Naval Hospital, Bethesda.

Serum hexosaminidase B levels progressively increase in pregnancy. With over 200 patients studied, there is a statistically significant increase ($p < 0.01$) in enzyme level in patients with excess weight gain (> 5 lbs/month) above normal pregnancy levels at 0-20 weeks gestation. From 20-30 and 30-40 weeks gestation, the increase in the enzyme level is significant ($p < 0.05$). Repeated analysis in patients with elevated serum enzyme levels in the first 20 weeks of gestation indicates persistent elevation of enzyme levels in the presence of normal weight gain. Presently this group is being studied with repeat enzyme determinations and liver profile studies, with careful monitoring for toxemia of pregnancy, in an attempt to profile biochemically the high-risk patient for toxemia of pregnancy.

CICC 2-06-347

A DOUBLE-BLIND COMPARISON OF CLOTRIMAZOLE WITH NYSTATIN FOR THE TREATMENT OF CANDIDA ALBICANS VAGINITIS. W.J. Jones, Jr. Naval Hospital, Portsmouth, Va.

This study will evaluate the use of a new vaginal drug, Clotrimazole (b5097) in the treatment of mycologically proven *Candida albicans* vaginitis.

To date 15 cases have been completed.

CICC 3-08-161

VAGINAL HYSTERECTOMY — A SIMPLIFIED APPROACH. R.F. Kirk and C.C. Scott. Naval Hospital, Philadelphia.

A consecutive series of 50 patients have had a vaginal hysterectomy performed using a modified posterior approach. The posterior cul-de-sac is entered initially; supporting uterine ligaments are divided and ligated in the posterior half and surgical attachment as an initial step. Vaginal incision in the remaining anterior half of the surgical field is then made. The remaining uterine support and the uterine artery are ligated as the bladder is dissected off the lower uterine segment. The anterior cul-de-sac is entered late and the adnexal pedicles are ligated by an automatic stapling device.

CICC 2-05-622

RELIEF OF POSTPARTUM BREAST DISCOMFORT. R.F. Kirk and N.W. Taylor. Naval Hospital, Philadelphia.

Patients involved in the study are seen in postpartum rounds by the ward medical officer and the nurse monitor assigned to collect the data for the study. To date 14 patients have volunteered for the quinestrol (a new steroid) study. Ten patients have delivered and have been enrolled in the study.

Results: Three patients have not had any breast enlargement or discharge. Five patients have had minimal enlargement and/or discharge. One patient had considerable discomfort from enlargement and discharge.

CICC 3-05-175

A SEROLOGICAL AND CLINICAL SURVEY OF PREGNANT WOMEN FOR TOXOPLASMOSIS. D.G. Martin and F.S. Billingsley. Naval Hospital, Bethesda.

The purpose of this study is to establish the incidence of toxoplasmosis in women during pregnancy, in this area, and the role of toxoplasmosis in congenital disease.

Approximately 3000-4000 women will be tested twice during pregnancy and again at the time of delivery. A cord-blood sample will also be collected from all newborns. Each sample will be tested for *Toxoplasma* antibodies by the indirect hemagglutination technique using tanned sheep erythrocytes sensitized with the antigen. Follow-up samples will be taken from mothers and babies who show significant titers.

During the period 1 Jul 1972 to 1 Jan 1973, 1,220 pregnant women have been tested, resulting in 8.0% (97) with positive titers for toxoplasmosis. Of these, 7.6% (47) have had positive maternal titers at the time

of delivery and 7.5% (43) of the babies have had positive cord blood. The data obtained to date suggest that the incidence of the disease in pregnant women for this area is not as prevalent as indicated by Stern, *et al.*, who reported an incidence of 4-6 per thousand, half of which infected the newborn. Although no apparent acute or chronic infection of mother or child has been established from this study to date, additional patients need to be tested in order to have more significant findings. Follow-up titers on all serologic-positive newborns for a minimum of six months is essential before congenital disease can be ruled out.

CICC 3-06-126

USE OF PARAMEDICAL PERSONNEL TO PERFORM ROUTINE MEDICAL SERVICES ON MILITARY PERSONNEL AND DEPENDENTS. C.C. Scott and R.F. Kirk. Naval Hospital, Philadelphia.

Our purpose is to find a registered nurse (RN) or licensed practical nurse (LPN), not currently employed and evaluate how easily, quickly, and efficiently this individual can be taught routine outpatient obstetric and gynecologic procedure. Using on-the-job training technique, this individual is to be taught by a senior resident or staff physician how to take an obstetric and gynecologic history, how to perform routine pelvic examinations, obtain Pap smears, offer birth-control advice, and do routine prenatal care. Eventually and hopefully, after about three months' training, this individual would be able to see her own patients with minimal physician supervision. Patient acceptance is to be evaluated.

We have evaluated one RN with generally favorable results.

CICC 2-05-604

TREATMENT OF DYSPLASIA AND IN-SITU CARCINOMA OF THE CERVIX WITH CRYOSURGERY AND CO₂ LASER BEAM. R.T. Upton. Naval Hospital, Portsmouth, Va.

During the past three years of a continuing clinical evaluation, now four years in continuity, cryosurgery has been used as a therapeutic modality in the management of selected cervical intra-epithelial neoplasias. Patients with atypical cervical cytology, colposcopically directed biopsies diagnostic of no more than intra-epithelial neoplasia, and endocervical curettage negative for neoplasia, have been treated with liquid freon cryosurgical techniques. The three-minute freeze procedure has been most recently utilized. Depending on the patient's desires for continued reproductive capability,

follow-up has included three-month interval reevaluation with colposcopy, cytology, biopsy and refreeze or hysterectomy.

At the first review, cryosurgery successfully cleared the neoplastic process in 81% of the patients so managed. A second-stage review of results is to be started shortly. The success rate appears to be approaching 88%. The use of lower temperature refrigerants such as N₂O can be expected to further improve the results. A cogent facet of this investigation has been the avoidance of all but a very limited number of conizations in the diagnosis and management of intra-epithelial cervical neoplasia. The use of colposcopically directed CO₂ laser-beam therapy will be started as an extension of this study, comparing the results with those of cryosurgery.

CICC 2-08-501

EVALUATION OF POST-DUE OBSTETRIC PATIENTS. R.T. Upton, J. Sebastian and J.O. Goodwin. Naval Hospital, Portsmouth, Va.

Our purpose is to achieve more uniform care of the post-due patient and to detect patients at risk with post-mature fetuses.

Patients in their 42nd week of gestation were evaluated with fetogram study and 24-hour urine test for estriol excretion. Patients in their 43rd week were evaluated with amniocentesis examination for meconium and maturity studies including: optical density, creatinine, and percent of fat cells. A fetal maturity score was used as presented in Sept 1971 OB-GYN, as criteria for induction of post-due patients.

Fifty-six patients with successful completion of amniocentesis were included in the study. Only two patients were found to have meconium-stained fluid. There were no intra-uterine deaths or neonatal deaths; however, there were three cord accidents necessitating emergency cesarean section. It was felt that the most common etiology for being overdue in our obstetric population was inaccurate dating. The greater incidence of iatrogenic morbidity was felt to outweigh the information gained from routine amniocentesis in the 43rd week of gestation, if the estriol excretion is in the normal range.

CICC 3-08-084

ANDROGENIC FUNCTION IN FEMALES WITH POLYCYSTIC OVARY SYNDROME. R.L. Weinstein, T.A. Daane and R.E. Reitz. Naval Hospital, Oakland.

Four virilized females with polycystic sclerotic ovaries were studied with (1) dexamethasone (DXM)

suppression (3 mg daily x 2 days); and (2) continued DXM suppression with chorionic gonadotrophin (HCG) stimulation (5000 I.U. daily x 4 days). Plasma testosterone (T) was measured for base line levels and, at the end of each period, by a double isotope derivative method. These studies were carried out before and after wedge resection of the ovaries. (Three normal ovulating control women were also studied.) The control subjects showed no significant suppression or stimulation of plasma T whereas the patients revealed the following tabulated results:

Conditions	Pre-wedge T (ng%*)	Post-wedge T (ng%*)
Base line	108 ± 24	97 ± 26
DXM	115 ± 19	87 ± 23
DXM HCG	285 ± 74	210 ± 70

*nanogram

The patients all had return of cyclical "ovulatory" menses following wedge ovarian resection, as determined by basal body temperature chart and endometrial biopsy.

An ovarian biochemical abnormality is suggested in these patients since pre- and post-wedge resection suppression and stimulation tests gave similar results, and all patients revealed significant stimulation of plasma T with DXM and HCG.

CICC 2-48-205 (also MR041.20.01-4001, in Endocrinology Section)

GONADOTROPIN PATTERN RESPONSIVE TO CLOMIPHENE CITRATE. J.F. Wurzel, T.A. Daane, R. Mastin and A.F. Parlow. Naval Hospital, Oakland.

The gonadotropin patterns of peri-menopausal patients after the onset of menstrual irregularities and hot flashes have not been reported. It is therefore planned to study daily serum (5-8 cc of blood) levels of FSH and LH in patients for a period of 20 days. The correlation of the fluctuation of serum gonadotropin with hot flashes in these patients will provide some useful information.

During the past several months six peri-menopausal women have been studied with serial daily serum measurement of gonadotropins. Clomiphene citrate (Clomid) was administered, 100 mgm daily for five days. The serum sampling continued through the period of Clomid therapy and for ten days thereafter. Samples are in the laboratory awaiting gonadotropin determinations. Upon completion, the results will be analyzed and reported.

MR041.20.01-4001

HYPOTHYROIDISM OF PREGNANCY AND FETAL SALVAGE. J.F. Wurzel, T.A. Daane and W.F.

McKenzie. Naval Hospital, Oakland.

All prenatal patients with no previous history of thyroid disease and less than 18 weeks' gestation, who were to be followed throughout pregnancy in our clinic, were screened with an initial T₄ (thyroxine) by column. If the initial and repeated values were less than 5.0 µg%, a complete thyroid battery was obtained and the patients were enrolled in the study. In the double-blind study, a placebo or thyroid (Euthroid, Warner-Chilcott Laboratories), two grains daily, was employed.

Thirty patients are enrolled in the study and 14 completed studies were submitted for analysis. Pre-treatment base line mean T₄ values are similar in the placebo (3.8 ± .13) and Euthroid (3.9 ± .14) groups. Repeated T₄ values at 28 weeks' gestation (placebo 4.8 ± .28, Euthroid 6.3 ± .41) show a significant difference; p < .05. At 36 weeks' gestation (placebo 5.2 ± .31, Euthroid 6.4 ± .23) a significant difference of the mean T₄ values was noted (p < .01).

Addition of Euthroid, 2 grains daily, significantly raises T₄ by column values at 20 and 36 weeks in patients with initial low values in pregnancy. Only after analysis of the total projected case study (100 cases) will a conclusion be drawn regarding fetal salvage.

CICC 2-48-204

CYTOLOGIC EXAMINATION OF CUL-DE-SAC ASPIRATES. J.A. Yauch and R.F. Kirk. Naval Hospital, Philadelphia.

Forty-two culdocenteses were performed in early 1972 on minor procedures in the operating room. Cytological exam was performed on all fluids obtained and 32 were Class I (normal). In the remaining ten specimens, not enough cellular material was present for adequate interpretation.

CICC 2-05-623

OPHTHALMOLOGY

HISTOLOGICAL ROUTINE EXAMINATION OF AUTOPSY EYES IN MILITARY PERSONNEL. B.R. Blais and M. Cowen. Naval Hospital, Philadelphia.

Information in ophthalmic pathology, with clinical pathological correlation, will be gained from the study of eyes at the time of autopsy. This will permit a correlation between the ophthalmic pathology findings

and the other general pathologic changes noted as part of the routine autopsy protocol. Much information on ocular pathology in post-mortem patients is needed.
CICC 2-05-425

AN INVESTIGATION OF THE MILITARY APPLICABILITY OF AN AUTOMATED VISUAL FUNCTION LABORATORY. D.G. Boyden and B.R. Blais. Naval Hospital, San Diego.

Our objective is to test the concept of a "Visual Measurement Laboratory" and develop a prototype unit which could be incorporated in any automated multiphasic health-testing system. A prototype Visual Measurement Laboratory will be instituted at the San Diego Naval Hospital and Regional Medical Center, as part of an automated multiphasic health-testing system.
MR305.05-3084

A CLINICAL STUDY OF A DISTINCT TYPE OF EYE DISEASE IN MILITARY PERSONNEL. D.G. Boyden, R.L. Marlor and B.R. Blais. Naval Hospital, San Diego.

Foveomacular retinitis is a distinct type of eye disease involving primarily the fovea (portion of retina responsible for central vision). It occurs predominantly in young, enlisted, military personnel, usually involves both eyes and results in permanently impaired central vision. It is the objective of this study to evaluate systematically all patients referred to the San Diego Naval Hospital with this disease. A complete ocular examination will be conducted with emphasis on special ocular diagnostic tests, including fluorescein-angiography photography, and static and kinetic visual fields; control models will be selected to help define the current status and the progression of the disease process. We now have case histories on 500 patients; 55 were admitted to Naval Hospital San Diego during this past year for treatment and study. We are starting to reexamine the Temporary Disability Retired List (TDRL) personnel for 18-month follow-up. The number of patients examined is small and no conclusions are available at this time.
M4305.05-3064

VISUAL ELECTROPHYSIOLOGICAL RECORDING SYSTEM. D.G. Boyden and C.T. White. Naval Hospital, San Diego.

The objectives of this study are to develop a simplified system for obtaining records of certain electrophysiological events which are produced by visual

stimulation, especially the visual-evoked cortical potential (VECP) and the electroretinogram (ERG). The system will be used by the Ophthalmology Department of Naval Hospital San Diego, for the study of certain macular diseases and other conditions affecting visual efficiency, and to develop the minimal system which will provide the data required. It is expected that commercially available components will be used for the most part, but certain highly specialized bioengineering components, such as some of those developed by NASA at Ames Research Laboratory for the physiological monitoring of the astronauts, may be specially fabricated for this purpose.

All major equipment has been procured. The complete system is nearing operational status; the specialized components are in the process of being checked on healthy individuals. The first patients to be studied for specific macular diseases will be processed in the near future.
M4305.05.3077

EFFECTS OF NORMAL LABOR AND DELIVERY ON INTRAOCULAR PRESSURE IN HUMANS. D.G. Boyden, T.O. Paul and J.B. Lench. Naval Hospital, San Diego.

Intraocular pressure (IOP) is thought, but not known to increase significantly during labor; if this could be documented, a valid indication for cesarean section in women suffering from recent penetrating ocular trauma or certain corneal diseases could be established. Thirty normal unselected pregnant women will undergo measurements of IOP by applanation tonometry during labor and delivery.

Preliminary work with a Tonomat tonometer on 12 patients indicates that a significant rise in IOP, from 15 mmHg resting pressure to a maximum of 48 mm Hg, does take place during uterine contraction with Valsalva's maneuver. Due to technical difficulties encountered with the Tonomat, as reported in the last progress report, an electronic tonometer (McKay-Marg) was obtained. This is now being standardized against the Tonomat, and further measurements will be made exclusively by the electronic tonometer.

IOP in labor increases significantly during uterine contraction and Valsalva's maneuver. Cesarean section is indicated in pregnant women undergoing labor in the face of recent perforating ocular injury, intraocular surgery, or Terrien's marginal corneal dystrophy.
CICC 2-16-401

THERMAL CYCLODIALYSIS: A NEW SURGICAL TECHNIQUE FOR THE TREATMENT OF GLAUCOMA. D.L. Brooks. Naval Hospital, Philadelphia.

The problem of improving upon the standard cyclo-dialysis with the thermal cyclo-dialysis has been attempted by performing the standard operation on one eye of a kitten and the thermal cyclo-dialysis of the fellow eye. Since these eyes are not glaucomatous, two parameters were chosen to compare the results of each operation. The first is by tonography and the second is by histological patency of a cyclo-dialysis cleft. In order to evaluate long-term tonography results, no operated kittens have been sacrificed to this date.

During the preceding year several modifications of the new procedure have evolved so that the technique now has been finalized. The search for this technique has been a major problem that now appears to have been solved.

The preliminary data with the standard cyclo-dialysis operation on many eyes show an initial increase in the coefficient of outflow with a moderately rapid tendency to return to the preoperative level. The increase in the coefficient of outflow with the thermal cyclo-dialysis is much greater than with the standard cyclo-dialysis and has a much slower drift toward the preoperative levels.

The preliminary data show the modified thermal cyclo-dialysis to be more effective and more lasting in increasing the outflow facility of normal kittens' eyes. CICC 2-05-611

CYCLOPLEGIC AGENTS — A RATIONAL APPROACH TO THEIR USE. J.C. Cole and F.H. Reeser. Naval Hospital, Bethesda.

The cycloplegic effects of atropine 1% and Cyclogyl 2% have been studied and compared in 25 patients according to protocol. Thus far, there has been no noted clinical difference in these two cycloplegic agents as far as their cycloplegic effects are concerned. But, 25 additional patients should be studied in order that a significantly large population may be included for meaningful statistical correlation and comparison. CICC 3-06-134

DIURNAL INTRAOCULAR PRESSURE VARIATIONS IN NORMAL SUBJECTS AND HOSPITALIZED PATIENTS. R. Stone and R. Olson. Naval Hospital, Bethesda.

The object of this study is to determine whether or not diurnal variations in intraocular pressure are reproducible in the same subjects on different days. The

McKay-Marg tonometer will be used to measure repeated applanation pressures. To date sufficient data are not available to make any progress report. CICC 3-06-133

ORTHOPEDICS

TREATMENT OF TIBIAL FRACTURES WITH ELECTRIC MICROCURRENT. G.W. Cady, J.M. Casey and C.T. Brighton. Naval Hospital, San Diego.

Stress (fatigue) fractures of various bones occur in about 4% of military recruits and take several weeks or months to heal. We are studying the accelerated healing of these fractures by local administration of electric microcurrent to a selected group of stress fractures involving the upper tibia. These patients will have a direct electric current (about ten microamperes) administered to the affected leg through a K-wire cathode inserted into the fracture site under local anesthesia. The anode of the small battery pack is taped to the skin and a nonweight-bearing cast is applied. Physical and X-ray examinations will be repeated periodically until clinical evidence of complete healing has occurred.

Since initiation of the project, four patients have been treated by this technique. All have returned to full duty. This is a cooperative effort and a double-blind study; no results or conclusions have been reached as yet. All reports have been forwarded. M4305.05-3079

THE DEGENERATIVE EFFECTS OF PARTIAL AND TOTAL RESECTION OF THE MEDIAL MENISCUS IN DOGS' KNEES. J.S. Cox, C.E. Nye, W.W. Schaefer and I.J. Woodstein. Naval Hospital, Oakland.

An experimental effort to determine the degenerative effects on the articular cartilages of the knee joint caused by meniscectomy was done by performing partial and total meniscectomies on the knees of dogs.

Only medial meniscus experiments were done and surgery was performed on both knees of 12 adult dogs for a total of 24 knee operations. Five knees were used as controls by simply opening and then closing the knee joint. In nine knees the medial meniscus was totally excised at the periphery. In ten knees the inner portion of the medial meniscus was excised leaving an intact peripheral rim. At intervals of 3-10 months the dogs were sacrificed and the knee joints were opened completely to allow thorough assessment of

the knee joints with respect to synovial reaction, articular cartilage changes, and regeneration of menisci.

Gross pathological changes revealed increased synovial and articular cartilage damage in those knees where total meniscectomies had been performed, even when there had been regeneration of a meniscus. Microscopic pathological specimens taken from the articular surfaces of the femoral condyles and tibial plateaus substantiated the gross pathological findings.

We have concluded that: (a) A meniscectomy leads to degenerative changes in the knee joint; (b) Partial meniscectomy leads to less severe degenerative changes; and (c) When meniscus regeneration occurred, the regenerated meniscus tended to protect the cartilage surfaces where it had regenerated.

CICC 3-48-182

BRACING FOR FEMORAL FRACTURES. D.H.

Gordon. Naval Hospital, Bethesda.

A study is being made to determine the effect of the quadrilateral socket ischial weight-bearing brace on stimulation of fracture-callus maturation and reduction of hospital stay. Thirty patients with femur and tibial fractures have been fitted with such a brace. For most closed fractures, fitting is done at six weeks after injury. Open fractures have required up to 24 weeks for fitting. An integral part of the program has been exercise in traction, as early as seven days after injury. All patients thus far have been studied retrospectively. A prospective study is being done.

There are only two cases of shortening after fitting with brace. One of these occurred after a refracture, and position was lost while the patient was in traction. The other patient lost 1.2 cm of length after fitting. All but one patient, with an open wound, have had good to excellent return in range of motion of the knees and hips.

In the prospective study, scanograms and external measurements are being obtained at the time of fitting and at intervals thereafter. Instead of restricting the study to open and complicated fractures, the study is being extended to some cases normally treated by surgery.

The quadrilateral socket ischial weight-bearing brace, in conjunction with a rigorous pre- and post-brace program, has been found to be a well tolerated method of stimulating fracture-callus formation. Good results are achieved and the method is being studied prospectively as an added form of closed treatment for these fractures.

CICC 2-06-319

REHABILITATION OF THE BELOW-ELBOW AMPUTEE UTILIZING THE BICEPS CINEPLASTY. L.H.

Luppi, R.W. Gorski, B. Munroe and R.L. Wilson. Naval Hospital, Philadelphia.

Fifty-one biceps cineplasties have been performed on patients with below-elbow amputations at the Philadelphia Naval Hospital during the years 1954 to 1971. This follow-up study will present an evaluation of 43 patients.

Sixty percent of the amputations were the result of war injuries. All patients were initially fitted and trained in the use of the conventional below-elbow prosthesis. Less than half of this group was selected for the cineplasty procedure. Those selected were mature intelligent patients with a functional elbow and good skin over the anterior arm. As the voluntary closing hook of the cineplasty prosthesis was not intended for heavy work, the patient's future employment must also be a prime concern. The major advantage of the cineplasty over the conventional prosthesis is that it permits voluntary graded motor control of the closing terminal device.

MR041.20.01-0346

TREATMENT OF ANKLE FRACTURES. M.A.

Maginnis. Naval Hospital Boston, Chelsea.

The purpose of this study is to assess the principle of rigid internal fixation and early motion as applied to fresh ankle fractures of various types. This method may improve on the functional end-result of ankle fractures treated by other methods. It cannot be determined whether the method employed is more effective than standard treatment methods, on the basis of present data.

CICC 3-03-062

CORRECTIONAL COMPRESSION OSTEOTOMY.

M.A. Maginnis. Naval Hospital Boston, Chelsea.

The purpose of this study is to assess a relatively new method of correctional osteotomy for residual deformities following fractures of the tibial shaft. The proposed correctional osteotomy was used in patients with well-healed but malunited fractures located proximal to the distal one-fourth of the tibia, with significant angular deformities; the patients complained of ankle or foot pain of a major or progressive nature.

After surgical exposure of, and drilling through the tibia, two stout Steinmann pins are placed, with the distal pin parallel and just proximal to the ankle joint, and the more proximal pin paralleling the knee joint. A two-thirds diameter wedge is removed from the

tibia; one limb of the wedge is completed as an osteotomy. The pins are brought parallel, and Charnley compression clamps are applied for approximately six weeks. The compression device and pins are removed at approximately six weeks and a weight-bearing cast is applied for support until bony healing. To date we have had two good results. The initial outlook is encouraging. The study is still in progress.

CICC 3-02-073

RESULTS OF CLUBFOOT TREATMENT. A.M.

Martinson and G.W. Cady. Naval Hospital, San Diego.

Long term follow-up of patients with congenital clubfoot, into adult life, has not been documented in the literature. Recruits with a history of clubfoot, from neighboring commands were evaluated by history, physical examination, X-ray studies and photographs. To date, 72 feet are included in the study.

Several preliminary conclusions appear justified: (1) Internal tibial torsion is not a part of the foot and ankle deformity complex; (2) All feet reaching maturity with significant residual foot deformity also present ankle-foot deformity, and (3) For this reason, triple arthrodesis, except as a late salvage procedure for very painful or deformed feet, does not in general give a good functional result.

When 100 feet have been studied, the data will be correlated and submitted for publication.

CICC 3-16-040

EVALUATION OF CERVICAL SPINE INJURIES USING CINEROENTGENOGRAPHY. C.W. Ochs, W.D.

Carver, J.B. Oldershaw and D.W. Cloos. Naval Hospital, Great Lakes.

Thirty-four patients with painful injured necks underwent radiologic examination of the neck in motion. Fifteen patients were examined by cineroentgenography; the others were examined by audio-video fluoroscopy. These studies were found to be invaluable in fracture management, diagnosis of instability, and in establishing solid healing.

Superior technical results were obtained using a high resolution 875-line monitor coupled to a two-inch quad-type video-tape recorder. The fluoroscopy was recorded with narration and was replayed moments later on the television monitor in the Department of Radiology, or edited later for staff conferences. Often the patient was shown the replay of his tape, which seemed to improve correlation and understanding of his management. The radiation exposure using the video-tape system was considerably less than with the "cine"-

system. In addition, the patients were examined in the standing position, allowing a greater degree of comfort during the examination. Examinations took less time to conduct, and simultaneous audio track narration was found to be extremely useful.

CICC 2-13-004

EVALUATION OF THE INCIDENCE OF CONGENITAL HIP DISEASE IN THE NEWBORN. A.L. Rehme.

Naval Hospital, Jacksonville.

As of 1 Mar 1972, 2,475 newborn infants have been examined by the Orthopaedic Service for the presence of an Ortolani's sign within the first 36 hours of birth. Twenty-four patients have been detected with a positive Ortolani's sign, which continues to represent an incidence of about 1%. The infants have all been treated with our abduction splint for three months.

The statistics to date are bearing out the observation that the incidence in females, as compared to males is four to one. It is predominantly a problem in Caucasian infants and there is definitely a higher incidence found in breech deliveries and patients with a family history of the disease.

At this time we are using our original splint initially, which immobilizes the child well; X-ray studies in the splint show the hips to be reduced, even in those with frank dislocations. When the child outgrows this splint, we apply a second style which permits a little more activity and facilitates cleaning. These two splints in combination appear to be more than satisfactory for our needs and cost only \$8.00 per splint.

An interesting by-product of our study has been the early detection of foot deformities and other orthopedic problems in the newborn infant, allowing early correction and treatment of conditions that might have been missed or neglected had it not been for our daily observations in the nursery.

CICC 2-8-523

A COMPARATIVE AND CORRELATIVE STUDY OF CLINICAL, ARTHROGRAPHIC AND ARTHROSCOPIC DIAGNOSIS IN KNEE PROBLEMS WITH FINDINGS AT SURGERY. E.F. Quinn, F.R. Nelson,

J.F. Lovejoy and D.Q. Wilson. Naval Hospital, Bethesda.

Arthroscopy and arthrography are being compared with clinical preoperative evaluations to determine the relative accuracy and effectiveness of these two tools. All patients coming to the outpatient service are being screened by a standard questionnaire, supplemented by a history and physical examination conducted by the

physician. More than one physician may examine the patient. Clinical diagnoses are made by all examiners and the data are retained by a reference-code method which is MTST (magnetic tape selectric typewriter) compatible. If a sufficient amount of time has transpired from initial examination to time of surgery, the patient is reexamined by the questionnaire and one or more examiners. All cases will have arthrography done by the Radiology Service, which diagnosis will be made without the aid of history, physical examination or clinical impression of the orthopedist. All operative cases will have arthroscopy immediately prior to surgery. The resultant impressions derived from each technique will then be compared.

Since the study is in its early phase, meaningful data cannot be offered. The technique developed in obtaining the history is useful in that it gives information directly translated to the patient's record. In summary, the authors have just established a clinical data retrieval system for comparing the relative accuracy and effectiveness of the clinical examination, arthrogram and arthroscopy studies in knee injuries.

CICC 3-06-224

DIAGNOSIS OF EARLY ARTHRITIS BY JOINT SCINTIPHOTOGRAPHY. G.J. Weir, Jr., and R.E. Easterday. Naval Hospital, Great Lakes.

Scintiphotography of peripheral joints has been performed using ^{99m}Tc technetium pertechnetate. Ten patients who were undergoing brain imaging were studied as examples of normal. Five patients with Reiter's syndrome, five with rheumatoid syndrome, three with osteoarthritis and eight with undiagnosed arthralgic complaints have been studied. Scintiphotography readily distinguishes joints which are obviously clinically inflamed, as they concentrate radioactivity to a greater extent than normal. However, no distinguishing characteristics of any specific arthritic disease have been detected. The patients with arthralgias have all had normal scans.

The goal of the project was to determine if scintiphotography was abnormal in arthralgia and whether it could be used as an early diagnostic aid. Scintiphotography is normal in patients with arthralgia, therefore, it is not helpful as a diagnostic aid.

CICC 2-13-014

PLASTIC FOAM AS A PROSTHETIC STRUCTURE AND STUMP-FITTING MATERIAL. I.J. Woodstein. Naval Hospital, Oakland.

The study now includes materials other than low-exotherm polyurethane foam, in particular an ultra-violet curing polyester resin which has been used to fabricate several stump sockets.

Several foam structures for use in water sports, swimming (SCUBA diving) and water skiing have been fabricated. These units feature resistance to salt and fresh water and are functionally adequate for the intended purpose.

The goals of rapid individual and direct forming of stump sockets on the amputation stump are realized with the use of ultraviolet curing polyester resin in 1.5 hours from arrival of patient through trial walking; this compares with an estimated three hours for conventional methods. It should also be noted that conventional methods require several waiting periods for plaster to harden and dry so that the total-time span (but not necessarily the operator's time) is about 16 hours to accomplish the same work status.

MR041.20.01-0240

OTOLARYNGOLOGY

THE DETECTION OF MIDDLE-EAR FLUID BY IMPEDANCE AUDIOMETRY. T.E. Acomb, S.C. Weber, P. Hartman and R.W. Cantrell. Naval Hospital, San Diego.

We wish to determine the presence of middle-ear fluid that may be clinically undetectable. Patients with clinically apparent, as well as patients with suspected serous otitis media are tested with the Grayson-Stadler otoadmittance meter. The findings of this study, involving 45 patients to date, show that there is a highly positive correlation between the clinical presence of otitis media and an abnormal tympanogram.

Several patients have been found to have an abnormal tympanogram with clinically undetected serous otitis which was subsequently found on myringotomy. There is a very high positive correlation between abnormal tympanograms and the presence of clinically detectable middle-ear fluid. There is an insufficient number of patients with clinically unsuspected serous otitis and an abnormal tympanogram to warrant any specific conclusions at this time.

CICC 3-16-028

THE MEASUREMENT OF EUSTACHIAN TUBE FUNCTION USING TANTALUM POWDER. L.H.

Bowers and S.C. Weber. Naval Hospital, San Diego.

No easy safe method of radiographic evaluation of eustachian tube function has been developed at this time. The use of tantalum powder for radiographic evaluation has been explored in 20 dog ears. Tantalum was injected into the middle ears through the tympanic membrane. Radiographs were taken at periodic intervals to determine the clearance of tantalum from the ears through the eustachian tubes. Direct surgical examinations, as well as tissue biopsies of all middle ear mucosa were performed. Histopathological slides were prepared to determine any cellular changes secondary to tantalum. At present all but two ears have been surgically explored. None of the tissue slides have been examined at this time.

At this stage in the study it appears that tantalum powder does not readily move through the eustachian tube from the middle ear. This finding indicates that the middle ear is cleared mostly by gravity, through the eustachian tube instead of by ciliary action.

CICC 2-16-411

MIDDLE EAR COMPLIANCE AND ITS RELATIONSHIP TO MILITARY RELATED NOISE-INDUCED HEARING LOSS AND ACOUSTIC TRAUMA. J.

Chew, H. Shipman and R.W. Cantrell. Naval Hospital, San Diego.

The objective of the study is to determine whether there is any degree of increased middle ear compliance in patients with hearing loss secondary to acoustic trauma or excessive prolonged noise exposure. This combination is quite common in the military, especially in aviators and supporting personnel. These defects yearly cost the government thousands of dollars in disability payments and hearing aids. If a relationship between acoustic trauma and middle-ear compliance is demonstrated, this will offer the Navy an easy noninvasive technique for determining risk factors in susceptible personnel with reference to noise exposure. All servicemen at one time in their career have audiogram examinations. Using the Grayson-Stadler otoadmittance meter, middle-ear compliance can be measured in all personnel seen at this hospital who have audiograms. Correlating the results of audiograms, middle-ear compliance and noise-exposure history should provide new and productive data regarding susceptibility to noise-induced hearing loss in military personnel.

All equipment has been procured. Questionnaires have been printed for the patients to complete. The

first group of patients has been tested. Grayson-Stadler Co. will provide our research group with a full-day seminar to better acquaint the examiners with the otoadmittance meter.

MR041.20.01-0402

THE USE OF HELIUM IN THE TREATMENT OF CHRONIC OTITIS MEDIA AND ACUTE BAROTITIS. T.F.

Miller, P.R. Burkett, G. Strom and R.J. Trevino.

Naval Hospital, Oakland.

Forty patients have been treated. The average interval between treatments is three days, and patients are usually seen for a total of two to eight treatments. Criteria for selection of patients are: absence of acute infection, inability to perform Valsalva's maneuver, and absent or inadequate politzerization with ordinary air pressure. Results to date have shown more effective aeration of the middle-ear space than can be obtained through conventional methods. Further application of this technique in the clinical population is planned.

CICC 3-48-096

A STUDY OF ANATOMIC CHANGES IN THE MIDDLE EAR ASSOCIATED WITH NOISE-INDUCED HEARING LOSS. M.J.

Rensink, S.C. Weber and R.W.

Cantrell. Naval Hospital, San Diego.

The objective of this study is to correlate anatomic changes with noise-induced hearing loss and acoustic trauma. Histologic examination of temporal bones obtained from autopsies will be evaluated for changes in the auditory nerve and organ of Corti. Correlation will be made with the background of noise and acoustic trauma, as well as with clinical findings, including the audiogram in active duty and retired personnel. The temporal bone lab is in full operation.

Presently 21 bones are in various stages of preparation for histological study. Each set of bones exhibited premortem hearing loss and a documented audiogram exists for each set. To ensure quality control the histopathology technician has taken and completed the temporal-bone course at AFIP.

MR041.20.01-0391

NEW METHOD FOR ENDOLARYNGEAL STENTING OF SEVERE LARYNGEAL WAR INJURIES. R. Rish, R.W. Cantrell and S.C. Weber. Naval Hospital, San Diego.

The present methods of splinting injured larynges is by use of a finger cot stuffed with foam, foam block or rigid tubes. This treatment results in laryngeal stenosis, granuloma formation in the larynx and trachea, and impaired voice production due to damaged vocal cords. The method proposed for splinting the damaged larynges would avoid these problems by using a properly shaped splint made of a nonreactive material. This procedure has only been reported in the Russian literature. The preformed splints will be made by using dog cadaver larynges for molds. Several sizes will be cast and each size will be made of Silastic, Silastic foam, hard rubber, foam rubber, acrylic and Portex. The experimental dog will then have its larynx crushed and a moulded splint of the proper size will be used for the repair. At four weeks the splint will be removed. The airway and cord motion will be photographed with a movie camera for documentation. At a later date the dogs will be sacrificed and the total larynx and trachea will be submitted for histologic study.

All equipment has been ordered and has been received. Canine cadaver larynges have been obtained for stent molds. Stent material has been ordered. The microscope has arrived and the surgical procedures have commenced on the dogs.

MR041.20.01-0401

PATHOLOGY

EVALUATION OF COMMERCIALLY AVAILABLE KITS FOR RADIOIMMUNOASSAY. G.J. Weir, Jr. Naval Hospital, Great Lakes.

This project has evaluated commercial kits for applicability to routine laboratory determinations. As kits become available they are checked for accuracy, reproducibility, ease of performance and clinical usefulness. Accuracy and reproducibility of a direct measurement of free thyroxine (RES-O-MAT ETR, MALLINCK-RODT-NUCLEAR) was previously reported in detail. This test is now routinely used in place of the combined resin uptake and total thyroxine measurements. It was not, however, proven as accurate as the total thyroxine measurement, nor as useful in difficult cases.

Human Growth Hormone radioimmunoassay is offered routinely. It has proven necessary to run determinations at least monthly to maintain technician familiarity.

Angiotensin I is assayed to assess renin activity. This test was proven accurate and reproducible and is now offered as a routine clinical test.

Assay of IgE was briefly evaluated and the test appears satisfactory, but current clinical demand does not justify further exploration.

CICC 2-13-006

EVALUATION OF CLINICAL APPLICABILITY OF NEW AND NON-ROUTINE LABORATORY TESTS.

G. John Weir, Jr.; J.T. Lucas and D.J. Kelly. Naval Hospital, Great Lakes.

New laboratory tests are proliferating rapidly. Some prove useful in clinical diagnosis while others prove to be of little use, or simply add another method of testing without improving accuracy, sensitivity or selectivity. New laboratory tests of any variety are evaluated in this protocol which also offers a vehicle to personnel who wish to perform a brief study that does not justify a separate project.

The authors are evaluating: detection of Australia antigenemia by commercial radioimmunoassay kit; Vitamin B-12 assay by a commercial kit, and by a locally developed process; and corticoid measurements. The Australian-antigen test is reproducible and accurate. Sensitivity is not yet determined. Occasional "non-repeatable" positive reactions are noted. Vitamin B-12 assay by the commercial kit is reproducible, but values are systematically 20-30% lower than those determined by a commercial laboratory. The corticoid evaluation has just begun.

A staff nurse has begun an evaluation of double-void urines in the management of diabetes mellitus.

CICC 3-13-135

PATIENT CARE

AN INVESTIGATION OF THE MILITARY APPLICABILITY OF AN AUTOMATED VISUAL-FUNCTION LABORATORY. D.G. Boyden and B.R. Blais. Naval Hospital, San Diego.

The objectives of this study are to test the concept of a "Visual Measurement Laboratory" by developing a prototype unit which could be incorporated in any automated multiphasic health testing system, and to set up a prototype Visual Measurement Laboratory at the Naval Hospital San Diego, as part of the Regional Medical Center. This would allow an evaluation of a Visual Measurement Laboratory in the ocular

examination of active duty, retired and dependent patients as part of an automated multiphasic health-testing system.

The start of this project is being held in abeyance due to the recall of funds allocated for the equipment that is vital to the initiation of the program.

M4305.05-3084

DEVELOPMENT OF SPECIALTY TEAM SUPPLY BLOCKS AND PERSONNEL TABLES TO AUGMENT NAVY SURGICAL TEAMS. D.A. Murray, H.R.

Hensle and J.E. Lang. Naval Hospital, San Diego.

The objective of this study is to develop medical-allowance lists for the Navy Surgical Support Team, Ophthalmological-Surgical Augmentation Team, Maxillofacial-Surgery Augmentation Team and a Medical-Administrative Team. Manning tables for the latter three teams will be developed, prototype units will be procured, and packaging requirements and field-test blocks will be designed. An appropriate committee will evaluate present pertinent allowance lists and establish proposed specialty-team supply and personnel requirements. Material will be procured and processed into prototype blocks ready for development. Personnel will be assigned to Prototype Teams and accompany their blocks into a simulated field situation in a major training exercise, either with the Fleet or the Marine Corps. Dental and Otolaryngology Departments are developing specialty trays and packs to be packed functionally in mount-out boxes. Supply Division is completing the pricing, and organizing the listings of items for inclusion in the specialty blocks. We will soon request comments and suggestions from BUMED Field Branch and Code 49 concerning packaging. Procurement of the equipment and supplies for this project will be delayed until funds for support have been allocated.

M4311.01.1011

SCREENING OF PATIENT MEDICAL HISTORIES BY AUTOMATION. F.R. Nelson and D.Q. Wilson.

Naval Hospital, Bethesda.

A magnetic tape selectric typewriter (MTST) has been proposed as a potential method of obtaining medical histories from orthopedic patients, using standard questionnaire and answer formats.

A list of questions has been developed to present any given patient the basic questions generally asked by an orthopedist in obtaining a history of present illness. The replies to these questions were then formulated by reference code on magnetic tape, in such a

fashion as to produce a medical history similar to one obtained by a physician-patient interview.

Using a single questionnaire, two major problems were encountered in this format. Firstly, it was not possible to obtain a branching history. Secondly, the types of questions asked for various parts of the body were too numerous to incorporate into one questionnaire. These problems were solved by producing "specialty" tapes and questionnaires, oriented to the knee, hip, hand, foot, back, metabolic and general problems. Space has been allowed for recording physical examination, laboratory and X-ray study results, diagnosis, and treatment plans.

Information obtained in the format for the knee and metabolic problems is being retained for use in existing clinical investigations, and will act as a uniform data base. The investigators feel that this system will need adaption to computer methods, and thus the formats have been left open for adaptation to other hospital programs that are under development, at this and other centers. The authors feel the system would need conversion to computer methods to produce a reliable system of generating medical records and data.

M4305.05-3091

PEDIATRICS

A PROSPECTIVE STUDY OF PERINATAL MORTALITY AND MORBIDITY AT A MILITARY HOSPITAL.

G.C. Burris. Naval Hospital, Portsmouth, Va.

The main objective of this investigation is to determine whether or not prenatal care, race, and economic status affect perinatal mortality and morbidity. In a population with standard prenatal and perinatal care available to all patients, the effect of the variables of race and economic status upon morbidity and mortality are being studied.

During the four-month period studied thus far, there have been 1,363 total live births, 1,235 Caucasian and 128 Negro. The overall death rate was 6.6 per 1000 live births. The death rate among Negroes was 7.8 per 1000 and among Caucasians 6.4 per 1000 live births.

No conclusion has yet been reached concerning the affect of economic status upon mortality. The death rate in Negroes and Caucasians is about the same in the population sampled, up to this time.

CICC 3-08-087

A PROSPECTIVE COOPERATIVE STUDY INTO THE ETIOLOGY OF REYE'S SYNDROME AND THE EFFECTIVENESS OF CURRENT MODES OF THERAPY. **M.N. Goldschmidt.** Naval Hospital, Jacksonville.

Since the beginning of the study on 1 Jan 1972, four cases of Reye's syndrome have been diagnosed and treated at collaborating military hospitals, with two intact survivors. To effect early referral of new cases, a recent mailing went out to over 150 departments of pediatrics in the uniformed services facilities describing the disease and our study, and establishing communication between these facilities and the nearest collaborating hospital (27 in continental U.S.). Over 45 of these facilities have agreed to refer cases to our study and the level of interest remains high.
CICC 2-30-336A

QUANTITATIVE NEWBORN GASTRIC CULTURES. **P.J. Goscienski.** Naval Hospital, San Diego.

In a search for a method by which the risk of sepsis can be ascertained in neonates, quantitative bacteriologic cultures have been performed on approximately 160 samples of gastric contents obtained from infants at the time of delivery. Giemsa and gram stains were performed on all specimens. Results were compared with birth history and the "septiscore," by which point values are assigned to pertinent historic and observational data.

In 95 infants in whom complete data are available, gastric cultures have shown no growth. There have been no cases of amnionitis or of documented infant sepsis in this group. The risk of complications and the incidence of positive cultures may have been altered by the frequent use of antibiotics in mothers with prolonged (greater than 12 hours) ruptured membranes.

Comparison reading strongly favors the gram over the Giemsa stain in evaluating the presence of cells and bacteria in gastric contents. Quantitation of neutrophils is of questionable value because of the unhomogeneous character of newborns' gastric contents. Further conclusions are not warranted at the present time.
CICC 2-16-413

PULMONARY COMPLIANCE IN THE NEWBORN PERIOD. **A.J. Griffin.** Naval Hospital, Great Lakes.

Pulmonary compliance and its evolution during the newborn period have never been adequately documented. A total body plethysmograph has been designed for an infant and is nearly completely constructed.

Data collection will begin when the equipment is operable.
CICC 3-13-163

SERIAL MEASUREMENT OF IgE DURING THE FIRST YEAR OF LIFE. **T.G. Groshong, C.B. Carter, M. Bazara, R. Miller and R. Hamburger.** Naval Hospital, San Diego.

Investigation of normal values of serum IgE in the first year of life and manner of inheritance is being conducted in 50 normal neonates and their parents. IgE levels were determined by radioimmunoassay.

IgE levels at six months of age show only three out of 50 children with over 10 μ /ml; normal distributions of IgE values (mean 17 μ /ml) were observed in adults.
CICC 3-16-054

MICROBIOLOGICAL SURVEILLANCE OF LEUKEMIA PATIENTS. **H.M. Koenig, J.A. Campbell and P.J. Goscienski.** Naval Hospital, San Diego.

Microbiological monitoring of all children receiving chemotherapy for acute leukemia or solid tumors, at this hospital is continuing. Cultures of the throat, rectum, blood and urine are taken at the time of the child's routine clinic visit. If infection is suspected, cultures of the site of involvement are included. Cerebrospinal fluid cultures are performed whenever signs of central nervous system involvement occur.

Thirteen children have now been cultured on this program. Four children have died from complications of their primary disease. Two of the children died from infectious complications. One child died from a staphylococcal enterocolitis. *Staph. aureus* had been isolated on several occasions during the four weeks preceding her demise, during which period she had been markedly immunosuppressed. The other child had *Staph. aureus* isolated from throat cultures for two weeks prior to her death. This child had a *Staph. aureus* septicemia at the time of death. The other two children died of hemorrhagic complications of their disease. Nine children currently being followed remain in clinical remission. Their total white blood cell counts are being closely watched and correlated with changes in microbiological flora during periods of leukopenia. We intend to treat vigorously, with appropriate antibiotics at the first sign of infection in any of these children.
CICC 2-16-415

EFFECT OF EARLY HYDRATION ON SERUM BILIRUBIN. W.L. McLean and T.J. Williams. Naval Hospital Boston, Chelsea.

The purpose of this study is to determine the effect of early hydration of the breast-fed infant with supplemental glucose and water. The study was modified after no statistical difference in mean bilirubin levels was observed between the control and study group in the first 50 infants investigated. For the second 50 infants, an infant formula was used for supplementation to study the effect of a solute load and water (vice water alone). The parameters studied include daily serum bilirubin, hematocrit and total serum solid levels, as well as weight losses and gains. Attempts to conduct long-term follow-up of neurologic and mental development findings have been frustrated by family moves due to military orders.

CICC 2-02-110

STUDY OF FOUR STRAINS OF SMALLPOX VACCINE: COMPARISON OF ROUTE OF ADMINISTRATION AND DOSAGE WITH MORBIDITY AND SEROLOGIC CONVERSION. J.E. Schanberger, P.J. Goscienski and J.D. Connor. Naval Hospital, San Diego.

The objective of this study is to evaluate four strains of smallpox vaccine in reduced dosage and to compare two routes of administration, in order to develop improved vaccination procedures and to reduce the incidence of complications attending primary vaccination. Since Nov 1970, 451 children received initial vaccination: 188 percutaneously and 263 subcutaneously.

Temperature of 101°F. or more, 4-14 days following vaccination, was associated with 30% of percutaneous and 18% of the subcutaneous vaccination groups. Vaccine-related complications occurred in 5% of percutaneous and 5% of subcutaneous vaccination groups. Morbidity (fever and/or complication) occurred in 32% of the percutaneous and 19% of the subcutaneous vaccination groups. Positive post-vaccination hemagglutination-inhibition titers, equal to or greater than 1:10, occurred in 64% of percutaneous and 82% of subcutaneous vaccination groups.

Fewer complications were associated with subcutaneous vaccination, and fewer complications followed standard percutaneous vaccination in individuals previously given subcutaneous vaccine.

M4305.05-3058

EVALUATION OF THE VECTORCARDIOGRAM IN EARLY DETECTION OF INCREASED RIGHT-HEART WORK IN ASTHMATIC CHILDREN. J.W. Thomas and W.L. McLean. Naval Hospital Boston, Chelsea.

The purpose of the study is to determine if the vectorcardiogram (VCG) can be used for the early detection of increased right-heart work in patients with asthma. After a complete history and physical exam, patients are skin tested with 72 common allergens and selected intracutaneous tests. Pulmonary function studies, sweat electrolyte determinations and indicated serologic tests are completed prior to vectorcardiography. After a statistically significant number of patients have been evaluated, the clinical findings will be correlated with the vectorcardiographic studies to determine whether early increased work load on the right side of the heart is demonstrated. At the present time, no final conclusions can be drawn, although no evidence of increased right-heart work has been found. The VCGs performed on eleven patients during an episode of acute asthma have all been normal.

CICC 3-02-067

A DOUBLE-BLIND CONTROLLED STUDY OF HEXACHLOROPHENE USAGE IN A NORMAL NEWBORN NURSERY. N.G. Tsoulos and P.J. Goscienski. Naval Hospital, San Diego.

This study was designed to answer the following questions in regard to hexachlorophene: (1) Does a bathing with a hexachlorophene soap decrease the incidence of staphylococcal disease in newborns, as well as decrease the colonization rate, (2) Do our current bathing procedures result in high blood levels of hexachlorophene, and (3) Is there any difference in neurological outcome and developmental status in infants bathed with, and without, hexachlorophene?

A hexachlorophene soap and a placebo soap will be used in a double-blind protocol. The nursery will be supplied with coded bottles of soap to be used on a specific day, randomized so that an every-other-day pattern will be avoided. This same soap will be used on the infant throughout his hospital stay. On the day of discharge, cultures of umbilical cord and nose, and a blood sample for hexachlorophene level will be obtained. At six weeks, a history for infections will be taken, and physical and neurologic evaluations will be performed. At six months of age, a Denver Developmental Screening Test will also be performed. The collective data will then be analyzed and correlations will be determined.

At this time, an insufficient amount of data have been accumulated to justify any conclusions.

CICC 3-16-023

EFFECTS OF EARLY FEEDING ON HYPERBILIRUBINEMIA OF THE NEWBORN. H.T. Yates, Jr., and W.S. Newman. Naval Hospital, Portsmouth, N.H.

The routine feeding schedule for newborns across the country is nothing by mouth for 12 hours prior to the first feeding with glucose water or formula. It has been suggested by G.B. Odell, and others that perhaps by feeding infants earlier, at four hours of age for example, their gut would be induced to excrete meconium and other gastrointestinal contents more rapidly. Dr. Odell suggests that the hyperbilirubinemia of the newborn may be a result of the enterohepatic circulation of bilirubin. If this is the case, the faster the gut is cleared of meconium the less likely are the infants to reabsorb bilirubin already secreted.

Our study has randomly selected normal infants to be placed into two groups. The experimental group is to be fed for the first time at four hours of age and the control group at 12 hours of age. Bilirubin levels will be checked in all infants on the birth date and then daily until discharge, using the A.O. bilirubinometer. To date, our results are too few in number to indicate which schedule is preferred to reduce hyperbilirubinemia of the newborn.

CICC 3-01-185

PSYCHIATRY

THE UNCONSUMMATED MARRIAGE: EVALUATION AND TREATMENT. W.J. Jones, Jr. Naval Hospital, Portsmouth, Va.

Twenty cases of nonconsummation of marriage have been seen, evaluated, and treated by the principal investigator during the past two years. Seventy-five percent (15) of the couples were relieved of their symptomatology by short-term, behaviorally oriented therapy. The remaining couples constituted therapeutic failures or required long-term therapy.

CICC 3-08-088

PSYCHIATRIC EFFECTS OF STRESS IN SPECIAL MILITARY OPERATIONAL ENVIRONMENTS. R.E. Strange, R.J. Arthur and E.K.E. Gunderson. Naval Hospital, Philadelphia.

Data collected by clinical psychiatric interviews and questionnaire administered to personnel in special stress military operational environments (a) prior to deployment, (b) during deployment on station, and (c) following deployment are reviewed. This is supplemented by follow-up clinical data on patients admitted to the psychiatric sick list from those special operational environments.

The study is being done in collaboration with the Navy Medical Neuropsychiatric Research Unit, San Diego, Calif.

M4305.07-3010

PULMONARY DISEASE

THE CLINICAL EFFICACY OF COMBINED "NON-SURGICAL" BIOPSY PROCEDURES IN THE DIAGNOSIS OF INTRATHORACIC LESIONS. R.C. Elliott, J.F. Smiddy and D.W. Shea. Naval Hospital, Bethesda.

This is a prospective study evaluating the efficacy of the concurrent use of all accepted "non-surgical" biopsy procedures for intrathoracic lesions. The techniques being studied include transthoracic needle aspiration and/or percutaneous puncture biopsy, endobronchial brush biopsy under guidance of bi-plane fluoroscopy, and transnasal fiberoptic bronchoscopy.

Over 500 patients have been studied with transnasal fiberoptic bronchoscopy. This is a new and enlightening procedure that is well tolerated by the patients, and allows clear visualization through the level of the tertiary bronchi. The superior optical system and excellent patient tolerance have allowed the investigators to develop diagnostic techniques that far outstrip the capabilities of the standard rigid bronchoscope. These positive features have recently been outlined in a 16 mm training film. Lesions at the subsegmental level are photographed and biopsied under direct visualization. The technique of subsegmental lavage has been developed to identify the site of hemoptysis. New techniques of bronchial biopsy are being developed, as well as a method of bedside bronchial aspiration for use in a patient in acute respiratory failure who requires uninterrupted support with a volume ventilator.

CICC 2-06-305

SPONTANEOUS PNEUMOTHORAX. T.A. Clark, D.E. Hutchison, R.M. Deaner and V.H. Fitchett. Naval Hospital, Oakland.

Spontaneous pneumothorax is usually a benign disorder caused by rupture of subpleural blebs or bullae, with compression of the affected lung. During most of the nineteenth century, and for the early part of the twentieth century, tuberculosis was thought to be the cause of this entity. Not until 1932, when Kjaergaard published his meticulous study, was the nontuberculous etiology fully appreciated. Seldom are the symptoms severe or life-threatening. Severe respiratory and cardiac insufficiency do occasionally occur, however, with the need for rapid relief of the pneumothorax. Our method of management and its supporting data are presented elsewhere.

CICC 2-48-201

PULMONARY FUNCTION SCREENING BY FLOW VOLUME LOOP ANALYSIS. H.N. Dean, L.A. Sheffer and J.L. Steffenson. Naval Hospital, Oakland.

The air flow velocity-volume (V-V) loop is a graphic representation of the flow of gas both into and out of the lung relative to the volume of gas in the lung at the moment. Equipment has been calibrated for analysis of pulmonary function by the V-V loop method, used in over 100 measurements of lung dynamics, compared to standard pulmonary function tests, and has been shown to be accurate and precise.

During the next year it is planned to conduct testing at the Army Induction Center, Oakland.

MR041.20.01-0336

A STUDY OF THE BACTERIAL CONTAMINATION OF HUMIDIFIED GAS IN A RESPIRATORY INTENSIVE-CARE UNIT. G.L. Koomos, Jr.; R.E. Brons; R.K. Baseman; and E.R. Mayes. Naval Hospital, Portsmouth, Va.

The purpose of the study is to quantitate the contribution of contaminated wall gas and entrained room air to hospital-acquired respiratory infections in a respiratory intensive-care unit. The procedures require 20 cu ft samples of gas and air using the TDL Particle slit sampler, B-1072-2 (Scientific Products), Culturette use for liquids, and Rodac plates (BBL) for surfaces. Background studies of the contamination of the unit are currently in progress.

These studies reveal that the wall oxygen and compressed air sources were free of contamination during a three-month study of weekly samples, and *Pseudomonas aeruginosa* was twice grown from room air over

a six-month period of daily sampling. *Pseudomonas aeruginosa*, as well as other species of non-fermenting gram-negative bacteria, and the fermenting *Enterobacteriaceae* have been isolated from the unit environment on many occasions. *Pseudomonas aeruginosa* has been isolated in one instance from humidifying equipment where the patient subsequently was colonized with *P. aeruginosa* of a similar pyocin type (pyorubin, red). *Pseudomonas aeruginosa* and *Pseudomonas maltophilia* were cultured from ice water, and the patient later grew a similar strain of *P. aeruginosa* (pyocyanin). All isolates of *Pseudomonas aeruginosa*, *maltophilia*, *stutzeri*, *putida*, and *fluorescens* are presently being maintained, along with patient isolates, for future typing where possible.

CICC 2-08-503

WORK OF BREATHING DURING CONTROLLED AND SPONTANEOUS VENTILATION. E.R. Lucier and J.J. Angel. Naval Hospital, Great Lakes.

Oxygen consumption was measured in patients in compensated respiratory failure at the time of weaning by means of a modified Collins spirometer. Oxygen consumption was measured first while the patient's ventilation was manually controlled, then during spontaneous ventilation. Along with these measurements, the tidal volume, minute ventilation and respiratory frequency were measured. Other measurements noted were room temperature, barometric pressure and patient temperature.

The patients were all initially placed on controlled ventilation, with 100% inspired oxygen concentration for at least 20 minutes, to achieve denitrogenation. The duration of assessment ranged from three minutes to ten minutes for each segment. While the controlled measurements were taken, each patient was urged to relax and was ventilated at a rate and tidal volume that precluded spontaneous ventilation. For the spontaneous state, controlled ventilation was stopped and each patient was urged to breathe.

Oxygen consumption, tidal volume, minute volume and frequency were all measured directly from the spirometer tracing and a drop in oxygen consumption was noted in 14 out of 15 patients on removal from the respirator. In only one patient was an increase of oxygen consumption demonstrated. No correlation was found between tidal volume, minute volume and frequency or ventilation equivalent, rate of oxygen removal and change from controlled to spontaneous ventilation.

CICC 2-13-012

EVALUATION OF PULMONARY EMBOLI AS PATHOPHYSIOLOGIC MECHANISMS OF PULMONARY DAMAGE AFTER TRAUMATIC INJURY.

M.J. O'Sullivan; J.W. Hammon, Jr.; and J.E. Lang.
Naval Hospital, San Diego.

Our objective is to investigate the mechanism of pulmonary injury after pulmonary embolization by autologous thrombi. Of interest was a series of animals with a denervated lung preparation in which the left lung reacted to the pulmonary emboli in a fashion different from the normal lung. When the emboli were directed toward the contralateral lung, the denervated lung gave a normal response in the vascular compartment; however, the pulmonary airway compartment failed to react with changes in either compliance or resistance.

It is suggested that the lung responds to emboli in a two-compartment fashion, the vascular compartment changing as a result of humoral factor, and the airway responding by an intrapulmonary reflex.

M4305.05-3072

LEFT VENTRICULAR DYSFUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE. D. Reid.

Naval Hospital, San Diego.

Patients with chronic obstructive pulmonary disease frequently manifest heart failure. The mechanism for this disturbance is, however, unclear. Some investigators implicate infection and pulmonary fibrosis resulting in pulmonary hypertension, while others believe that drastic shifts in ventilation and perfusion result in chronic arterial desaturation and cor pulmonale.

Patients with the established clinical and laboratory diagnosis of chronic obstructive pulmonary disease, after careful evaluation by history and clinical examination, will receive routine chest X-ray exams, laboratory studies, and electrocardiograms. By means of simple venous cutdown, a flow-directed balloon-tip catheter will be directed into the right heart chambers and pulmonary vasculature. Vascular pressure and cardiac output determinations (by Fick and green-dye methods) will be performed. Our objective is to evaluate the incidence, pathophysiologic mechanisms, and response to therapy of left ventricular dysfunction in patients with chronic lung disease; and concomitantly, to develop and evaluate feasible techniques for the accurate assessment of cardiac function in such patients, both with and without pressure ventilation. Major equipment pertinent to the study has arrived and supply items necessary for the project are expected shortly.

CICC 3-16-024

CONTINUOUS POSITIVE-PRESSURE BREATHING IN THE ADULT RESPIRATORY-DISTRESS SYNDROME AND COPD WITH ACUTE VENTILATORY FAILURE. D. Reid, R. Crafts, E.E. Bartimo and R.E. Bondurant. Naval Hospital, San Diego.

Continuous positive-pressure ventilation (CPPV) remains a controversial therapeutic entity in the adult respiratory-distress syndrome, primarily because clinical studies utilizing this therapy have either not measured oxygen transport, or the results have been inconsistent. CPPV application in human clinical situations has invariably shown that arterial oxygen tension increased, but whether or not this effect is offset by concomitant fall in cardiac output due to decreased ventricular filling, has not been properly assessed.

The simple purpose of this study is to determine whether or not oxygen transport is enhanced during CPPV for patients with the adult respiratory-distress syndrome and patients with acute ventilatory failure associated with COPD (chronic obstructive pulmonary disease). Adult respiratory-distress syndrome will be defined as: a compatible chest X-ray picture, lack of clinical congestive heart failure, a decreasing effective compliance, and an inability to attain normal arterial oxygen tensions (with inspired oxygen tensions of 50% or greater) utilizing conventional controlled intermittent positive pressure breathing (IPPB). The patient will then undergo a trial of controlled CPPV after determination of the magnitude of right to left shunting, pulmonary artery and pulmonary artery wedge pressures and oxygen transport, on conventional IPPB. Oxygen transport will be reassessed during CPPV and the ventilation mode for continued therapy will be determined by identifying the method with greater oxygen transport.

CICC 3-16-036

EFFECT OF AEROSOLIZED BRONCHODILATORS ON PULMONARY DIFFUSING CAPACITY. D. Reid. Naval Hospital, San Diego.

This study is designed to evaluate the effect of aerosolized bronchodilators (isoproterenol and epinephrine) on pulmonary diffusing capacity in man, as measured by the single-breath carbon monoxide technique. Diffusion abnormalities may be a cause of the arterial hypoxemia seen in patients with lung disease. Bronchodilators such as aminophylline and isoproterenol have been noted to worsen arterial hypoxemia in certain patients. Therefore, we plan to study approximately ten normal subjects and ten patients with preexisting lung disease. Pulmonary diffusion capacity, as measured by

the single-breath carbon monoxide technique will be performed before and after the administration of aminophylline and isoproterenol.

CICC 3-16-056

PHYSIOLOGIC INDICATORS OF STEROID THERAPY IN PULMONARY SARCOIDOSIS. **D. Reid and R. Schillaci.** Naval Hospital, San Diego.

Most patients with pulmonary sarcoidosis do not require any form of therapy. Therapy in the main, when administered, consists of oral steroids. Absolute indications for steroid therapy are few in number. The purpose of this study is to take a look at pulmonary physiologic parameters which may respond to steroid usage. All patients with a histopathologic diagnosis compatible with pulmonary sarcoidosis will undergo measurement of static and dynamic volumes, determination of VD/vt (ratio of physiologic dead space to tidal volume), and pulmonary mechanics studies.

Those patients with abnormal parameters will receive moderate doses of prednisone for 2-3 weeks. Subsequently, the patients are restudied in a similar fashion.

To date, 14 patients have been studied as outlined. Eleven patients had normal static and dynamic volumes and arterial blood gases. Three patients to date have been given moderate doses of prednisone for 2-3 weeks, because of significant pulmonary physiologic abnormalities in two patients, and because of significant ocular involvement in one case. The two patients with abnormal physiologic parameters manifested objective evidence of improvement. Further studies are indeed indicated to determine the validity of regarding abnormal physiologic parameters as an indication for steroid therapy in patients with pulmonary sarcoidosis.

CICC 2-16-428

EFFECT OF CHEST PHYSIOTHERAPY ON PULMONARY GAS EXCHANGE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE. **D.W. Shea and R.C. Elliott.** Naval Hospital, Bethesda.

In most hospitals much time is devoted to chest physiotherapy in the patient with chronic obstructive pulmonary disease (COPD). Previous published studies have shown no significant posttreatment improvement in flow rates or sputum production.

This is a prospective study of the efficacy of chest physiotherapy as measured by changes in alveolar-arterial (A-a) oxygen gradients, ratio of physiologic dead space to tidal volume (VD/vt) and diffusion of carbon monoxide (DL_{CO}).

To date, six patients with COPD have been studied. Three have shown improvement in all measured parameters of function; Two patients have shown no essential change, and; One patient showed decreased DL_{CO} and increased VD/vt ratio after therapy.

It is anticipated that chest physiotherapy will improve DL_{CO} , A-a gradients and VD/vt ratios in the majority of patients with COPD.

CICC 2-06-307

RADIOLOGY

CLINICAL EVALUATION OF A TIN ELECTRON FILTER FOR (^{60}Co) COBALT RADIATION THERAPY UTILIZING A THERMOLUMINESCENT DOSIMETRY SYSTEM: EFFECT ON SKIN SPARING. **J.L. Murray.** Naval Hospital, Philadelphia.

A Teledyne Isotopes thermoluminescent dosimeter (TLD) reader has been installed and is now operating in the Radiation Therapy Department. Preliminary measurements have been made using a masonite phantom. These measurements verify that the tin electron filter provides significant "skin-sparing."

The clinical portion of this study has been revised. Instead of demonstrating the effectiveness of the tin-electron filter by comparing skin erythema with and without the filter, an attempt will be made to show the effectiveness of skin-sparing as related to hair loss. This will require a patient who is to undergo whole-brain irradiation. Half of the treatment port will be shielded with the tin-electron filter. The hair under the portion of the treatment port without the filter should epilate sooner than the hair under the shielded portion. This will provide a more clear-cut demonstration of the skin-sparing effect than skin erythema.

Studies are tentatively scheduled to begin within the next month. At this time more TLD phantom measurements will be made to correlate the radiation dose with the clinical effects observed. As more patients come in for treatments of this type, more studies will be conducted.

CICC 3-05-176

EVALUATION OF TIME-SAVING POTENTIAL OF PERSISTENCE SCOPE. **C.P. Myers.** Naval Hospital, Great Lakes.

This study indicates that the persistence scope is not the most significant factor in reducing the patient positioning time; however, the persistence scope is

recommended for all hospitals with a Pho-Gamma camera. It was observed during the study that the scope proved to be a great confidence builder for the technicians (especially during training), and when a portion of the study was to be repeated, they were reluctant to position patients without using it. The technician confidence attained, the rapid visualization of thyroid nodules, flow parameters, and other advantages which were not in the scope of this study justify the purchase price.

The persistence scope was supplied with an 8 mm movie camera as an accessory for making single-frame records and dynamic-flow studies. No profitable use has been realized from this accessory, primarily due to the time required to have the film processed. Purchase of the movie camera accessory by other facilities is strongly discouraged unless the facility has in-house 8 mm-film processing. Even with local processing, it is doubtful that a significant use can be found for this accessory.

CICC 2-13-016

RECTILINEAR SCANNER-WHOLE BODY COUNTER.

Calvin P. Myers. Naval Hospital, Great Lakes.

A rectilinear scanner provides the basic instrument for use as a clinical whole-body counter while retaining its full use as a scanner. The minimum detectable activity which is determined by the background radiation is being investigated.

The background is approximately 1.4 cpm/cm^3 of detector. This relatively low background (0.2 to 1 cpm/cm^3 would be anticipated within a well shielded room) is due to the ample shielding around the detector which is provided for its normal use as a scanner. The minimum detectable activity for a point source of ^{57}Co on the axis of the detector was determined to be 0.01 uCi , with the source detector distance 50 cm . Because of high background at about $88 \text{ kiloelectron volts (kev)}$, which may be due to fluorescent X-rays from the lead detector shield, minimum detectable activity for energies above 300 kev should be improved about an order of magnitude.

CICC 3-13-140

EARLY DETECTION OF VENOUS THROMBOSIS WITH RADIONUCLIDE-TAGGED PLATELETS, FIBRINOGEN AND STREPTOKINASE. **J.M. Tullis and Q.E. Crews.** Naval Hospital, San Diego.

The objective of this study is the early detection of venous thrombosis with radioisotopes, resulting in prevention of sequela and shortened hospital stays. Leg

scans for venous thrombi will be done in any high-risk medical or surgical patient in whom thrombi are suspected or on patients who have a high probability of developing thrombi with the concomitant risk of pulmonary emboli.

In certain very high-risk patients, initial lung scans will be done to provide a base-line. Useful data about subclinical pulmonary emboli can be accrued in this manner. A comparison study will be done on modes of treatment and prevention. To date, insufficient data have been accumulated to justify any conclusions. CICC 3-16-037.

SURGERY — GENERAL

THE EVALUATION OF HYPOPHOSPHATEMIA AND BLOOD VOLUME CHANGES INDUCED BY PARENTERAL HYPERALIMENTATION. **E.J. Aucoin, C.R. Valeri and C.G. Zaroulis.** Naval Hospital Boston, Chelsea.

The purpose of this study is to determine the degree of phosphate depletion and the changes in blood volume presented by patients undergoing prolonged intravenous hyperalimentation. Patients are selected for intravenous hyperalimentation in accordance with the Intravenous Hyperalimentation Protocol. In addition to the initial laboratory determinations, certain studies are performed on a weekly basis, as well as pre- and post-hyperalimentation. Changes in blood volume have been noted to be associated with the trauma of surgery and/or with subsequent blood transfusion.

Patients on prolonged hyperalimentation exhibit little change in blood volume once the aforementioned factors have undergone resolution. Further, there has been a significant decrease in red cell organic phosphates in patients on intravenous hyperalimentation. New improved hyperalimentation solutions have been used recently which have minimized and/or eliminated the decrease in phosphates. Several patients who have been hyperalimented intravenously for prolonged periods, up to six months, are being followed and have remained remarkably free of significant changes in either blood volume or inorganic red cell phosphates. It is anticipated that the continued follow-up of these patients, along with new patients will provide further insight, especially with regard to prolonged intravenous hyperalimentation.

CICC 2-02-108

PERIPHERAL MUSCLE pH. F.P. Banda and R.L. Mullin. Naval Hospital Boston, Chelsea.

A laboratory and clinical study has been initiated to develop techniques that will facilitate the use of peripheral muscle hydrogen ion concentration (pH) measurements. Instrumentation Laboratory glass pH electrode No. 14183 has been utilized in conjunction with a digital pH meter and a potentiometric recorder. Preliminary studies have been carried out by placing the electrode on the extremity muscles of dogs and baboons during normal and hypovolemic states. The technique is feasible but careful attention must be paid to prevent poisoning of the small sensitive glass membrane with blood. Further laboratory and clinical studies are planned.

MR041.20.01-0397

A STUDY OF DEEP VEIN THROMBOSIS IN POST-OPERATIVE AND BEDRIDDEN PATIENTS USING IMPEDANCE PHLEBOGRAPHY TECHNIQUES: A PROSPECTIVE STUDY. R.S. Gold and B.M. Golden. Naval Hospital, Philadelphia.

Early diagnosis of deep vein thrombosis is essential to prevent fatal pulmonary embolism from the leg veins. A noninvasive technique, such as impedance phlebography, might be effectively used as a screening technique to achieve this end. (This is as opposed to radioactive-tagged fibrinogen or venography techniques which are invasive.) All admissions to the General Surgery Service at this hospital will be admitted to the study and followed through their pre-, intra-, and post-operative courses, using the impedance phlebograph in an attempt to diagnose as early as possible latent deep vein thromboses.

CICC 3-05-183

USE OF CEPHALOTHIN PERITONEAL IRRIGATION IN APPENDICITIS. R.S. Gold and S.J. Mucha. Naval Hospital, Philadelphia.

Although considered a benign surgical emergency operation, appendectomy is fraught with a considerable amount and variety of postoperative morbidity. The infectious complications of appendectomy performed for appendicitis are ordinarily localized processes and might be dealt with in a preventative manner by local means. This study will compare treatment of the local peritoneal site, evaluating the complication rate in irrigation with saline, irrigation with cephalothin and no irrigation. Approximately 150 cases will be analyzed. At this point, 30 cases are collected. With this

hospital's average of 164 appendectomies for appendicitis per year, over the past five years, the study should be easily completed.

CICC 3-05-184

EFFECT OF PARENTERAL HYPERALIMENTATION, INCLUDING INTRAVENOUS FAT, ON BODY WEIGHT AND NITROGEN BALANCE IN SURGICAL PATIENTS. G.W. Gregory and W.J. Fouty. Naval Hospital, Bethesda.

Biochemical, metabolic and endocrine responses will be used to demonstrate the feasibility and advantages of using a fat emulsion (*Intralipid*) in combination with other parenteral nutrients in intravenous hyperalimentation programs. A two-year study would involve 20 surgical patients not able to receive oral alimentation. By utilizing a fat emulsion in combination with a solution of amino acids (*FreAmine*) and carbohydrates, it is possible to administer 2600 or more calories per day, together with 12 to 14 grams nitrogen. A mixture of one liter 20% *Intralipid*, one liter 8.5% *FreAmine* and 500 cc of 20% glucose solution will be used to provide complete parenteral nutrition.

Metabolic responses will be assessed by accurate daily weight determinations, nitrogen balance studies, and close monitoring of various biochemical parameters. The endocrine response will be judged by following changes in the intravenous glucose tolerance test. Plasma assays for insulin and growth hormone, and plasma cortisol measurements will also be monitored.

CICC 3-06-179

ARTERIALIZATION OF THE VENOUS SYSTEM.

R.L. Mullin and H.W. Fegley. Naval Hospital Boston, Chelsea.

The purpose of this study is to reverse the arterial and venous flow in the canine hind limb. This is being evaluated with the anticipation of clinical application in the near future.

An ischemic leg is created in the canine and treated by forming an arteriovenous fistula, sending arterial blood to the ischemic extremity in a retrograde manner through the venous system. With perfection of the surgical technique, excellent results have now been achieved in the research lab. A proposal to put this procedure into clinical use in the hospital is being considered.

The laboratory results suggest that this procedure may be very beneficial to diabetics with advanced atherosclerosis of the small arteries.

CICC 2-02-104

TREATMENT OF ACUTE AND CHRONIC EDEMA SECONDARY TO LYMPHATIC OR VENOUS INSUFFICIENCY. R.L. Mullin and H.W. Fegley. Naval Hospital Boston, Chelsea.

The purpose of this study is to evaluate the use of the Jobst Intermittent Compression Unit in patients with acute and chronic edema. This apparatus has been used on 16 patients, 15 of whom received noticeable diminished edema with good symptomatic relief. Our results have been excellent. Hopefully, more patients will have this instrument made available to them. CICC 2-02-106

VIVONEX IN PREOPERATIVE BOWEL PREPARATION. R.L. Mullin and R. Pejic. Naval Hospital Boston, Chelsea.

The purpose of this study is to determine the acceptability of Vivonex (elemental diet/soluble powder) as a bowel prep for colonic surgery. Analysis of data on ten patients who were given Vivonex in preparation for colonic surgery revealed a 20% incidence of wound infection. Benefits of the Vivonex were that the patient could maintain a 2000 caloric intake up to the day of surgery. Colonic residue was minimal and not troublesome.

Retrospective analysis of 20 consultative patients undergoing colonic surgery with a conventional bowel prep revealed a 25% incidence of wound infection. Since Vivonex-treated patients fared no worse, and maybe better than the control group, a prospective randomized study was initiated in Nov 1971. To date five patients have entered the study. A study protocol has been printed and is to be an integral part of the management of all patients undergoing colon surgery. CICC 2-02-103

PATHOGENESIS OF ENDOTOXIN SHOCK IN MILITARY MEDICINE. R.W. Virgilio and J.E. Lang. Naval Hospital, San Diego.

The pathogenesis of endotoxin shock will be investigated from several viewpoints, including the possible mechanisms of intravascular coagulation, immune complexes and complement activation. Additionally, the role of cortisone in protecting experimental animals will be studied. The baboon (*Papio doguera*) has been selected as a larger primate that is ideal for studies of the mechanisms of endotoxin shock, and which allows for better correlation with human septic shock. Multiple physiologic parameters will be observed in controls, and following treatment with Arvin (pit viper venom), cobra venom factor, or cortisone.

Ten animals have been studied, four of which have been infused with 10^9 *E. coli* organisms; three are surgical controls, and; three have been pretreated with 3 μ /kg Arvin, 24 hrs prior to the *E. coli* infusion. The experimental animals are infused over a ½ hour period and blood is drawn for assay at base line, 0 time, + 1 hr, + 2 hrs and + 4 hrs of infusion.

There seems to be evidence of consumptive coagulopathy after *E. coli* infusion, with a decrease in platelet count, white blood cell count, fibrinogen level, and Factor VIII. This is accompanied by an increase in red cell fragility. Arvin does not seem to have any pulmonary protective effect. M4305.05-3066

SURGERY — ORAL

FEASIBILITY OF LIGHTWEIGHT EXTRA-ORAL MAXILLOFACIAL APPLIANCES FOR WAR INJURIES. D.N. Firtell, R. Anderson and M. Donnan. Naval Hospital, San Diego.

The objective of this study is to develop a lightweight, extra-oral maxillofacial appliance made of a durable and easily handled material that can be retained with ease by mechanical or adhesive means but still maintain adequate strength, durability, and esthetics necessary for fabrication of a prosthesis. We will study the feasibility of utilizing dimethylpolysiloxane (silicone rubber), of the type presently being used, mixed with a foaming type. We will determine what percentage of foam can be added and still maintain adequate properties. We will determine if a large prosthesis can be made with similar ease as a smaller appliance, and still maintain the desired properties. We are in the process of having the pneumatic press modified to our specifications and are procuring the necessary supplies. We have designed a special machine to cure the appliance material and it is being built at this time. M4305.04.3006

EXTRACRANIAL SUSPENSION VS. INTRAOSSEOUS AND INTEROSSEOUS SUPPORT IN THE TREATMENT OF FACIAL FRACTURES. W.R. Hiatt, W.E. Sugg and E.L. Mosby. Naval Hospital, San Diego.

Documentation and comparison of the many modalities in treatment of facial fractures is under study from several clinical views. Comparative analysis of extracranial fixation has included the Crawford and Irby head frames and biphasic appliance techniques.

Intraosseous support of fractures by closed and open reduction methods has been combined with suspension wire, transosseous internal and intermaxillary fixation. Multiple modalities of definitive therapy are frequently required to properly manage the more complex injuries. In-depth comparison and conclusions require an extended period of study in order that astute recommendations may be made.
CICC 2-16-416

EFFECTS OF ORTHOGNATHIC SURGERY ON THE TEMPOROMANDIBULAR JOINT. R.A. Lazaro and R.D. Jackson. Naval Hospital, Bethesda.

The purpose of this study is to determine the effects of orthognathic surgery on the temporomandibular joint. Information gained from this study may expose possible causes of postoperative problems encountered in this type of surgery. The anatomic study will be carried out using the Weinberg radiographic technique and the Deman pantographic recording system will be utilized in the functional study. This project is in its early stages and no findings can be reported.
CICC 3-06-225

POST-EXTRACTION ALVEOLITIS IN NAVAL PERSONNEL. H.S. Samuels. Naval Hospital, Oakland.

Although the incidence of alveolitis (dry socket) is not well established, available data suggest that 2% of all tooth extractions and 5-6% of all mandibular third-molar extractions are followed by this complication. Based on the current Navy population, it is estimated that 8,000 cases of alveolar osteitis occur annually. This results in an annual loss of 32,000 patient man-hours and an undetermined loss of personal efficiency due to associated morbidity. It is hypothesized that a reduction in the oral bacterial population, during the time interval in which surgery and subsequent clot formation occur, is a critical factor in the prevention of alveolar osteitis.

This project is about half completed and, purposely, investigators are not apprised of the results to date. We expect to continue in the same manner for at least another year. Data have been obtained on 912 patients and a total of 1,452 mandibular third-molar extractions. Alveolar osteitis was associated with 7.1% of the surgical extractions and 1.33% of the nonsurgical extractions. Data accumulated are not yet sufficient to permit testing the experimental hypothesis.
MR041.20.01-4001

INVESTIGATION OF COMPENSATORY SALIVARY GLAND HYPERTROPHY. H.S. Samuels. Naval Hospital, Oakland.

By gaining a high index of suspicion in finding such patients, hospital days would be reduced by eliminating or curtailing the need for detailed patient work-up.

A minimal number of dogs, and 400-500 gram rats will be used. The parotid and submaxillary glands in the rat and the parotid and mandibular (with its contained monostamotic part of the sublingual) glands will be used in the dog. The two major glands will be removed on one side under general anesthesia. The glands will be weighed and histopathologic examination will be performed. The animal will be maintained in the colony on a regular diet for a period of three to six months. At the conclusion of the appropriate time, the contralateral glands will be removed, weighed and subjected to histopathologic study. An attempt will be made to demonstrate contralateral hypertrophy which might mimic a tumor. Kodachrome photography will be used to document progress and results.
MR041.20.01-4001

MAXILLOFACIAL COMBAT CASUALTY REHABILITATION WITH BONE GRAFTS. H.J. Sazima, L. Gold and J.F. Kelly. Naval Hospital, Philadelphia.

Fifty-two mandibular autograft and allograft procedures were accomplished in an experimental dog model to evaluate treated and untreated graft materials. Grafts were applied to a surgically created inferior border defect. Untreated autografts displayed evidence of healing in four weeks with clinically demonstrable union and histologic evidence of osteocyte invasion. HCL surface decalcified, gas-autoclaved autografts showed 50% less union and decreased osteocyte invasion at the same interval. Results of allograft procedures suggest that carefully scheduled treatment by defatting agents and surface decalcification, along with lyophilization is necessary to prepare the allografts for optimal host acceptance.

In the model used devitalized teeth in the graft area were found to be a possible source of graft rejection. A new modification of this model has been developed to obviate this problem. With the exception of the dogs' mandibular-cuspid teeth, which were sectioned at the gingival margin, all other mandibular teeth were removed.

Inlay and onlay allografts prepared with various precise treatment schedules will be further evaluated in this model to determine optimum defatting and decalcifying intervals. Fractures will also be created, and

appropriately treated allografts will be evaluated as internal fixation devices.

MR041.20.02-0388

ALLOGENEIC TOOTH TRANSPLANTS: A CLINICAL INVESTIGATION. H.O. Scharpf and R.G.

Triplett. Naval Hospital Boston, Chelsea.

A clinical study of tooth transplants is being conducted over a period of two years to evaluate the feasibility of tooth transplants as an acceptable clinical procedure. Patients requiring the extraction of cuspid, bicuspid, and molar teeth are being screened and if acceptable, requested to participate in this study.

Autogenous transplantation of maxillary cuspid and mandibular-molar teeth are performed on patients with suitable indications. Allogeneic transplantations of donor bicuspid teeth (removed for orthodontic reasons) will be stored, endodontically treated and fluoridated, and then placed into a fresh extraction site of another patient requiring the extraction of a bicuspid tooth.

Patients will be followed for a period of five years with periodic evaluation. Early results have been very encouraging.

MR041.20.02-0404

SURGERY — PLASTIC

MAXILLOFACIAL INJURY WITH PALATE-DEFECT STUDY. G.W. Anastasi. Naval Hospital Boston, Chelsea.

The purpose of this study is the evaluation of methods for the treatment of maxillofacial defects involving the palate. The effects of surgery on the developing maxilla are being clinically determined and documented. The muscular anatomy of the palatal muscles in patients with congenital defects of the palate is also being studied. The effect of reconstruction of the palate with autogenous bone grafts and synthetic material is under evaluation. Our observation of the effects of surgery on the developing maxilla appears to indicate that the lateral growth of the maxilla is inhibited by this surgery. Autogenous bone grafting, if it is not to effect maxilla growth would probably be done as a secondary procedure on the palate, usually after the patient reaches the age of eleven years. Additional information is still needed to determine the effects of surgery and drugs on the developing maxilla. The effect of anxiety on the developing fetus, as a possible

cause of maxillofacial defects will also require additional exploration.

M4305.05.01-3017

ELECTRICAL STIMULATION OF BONE GROWTH IN BONY DEFECTS OF THE PALATE. G.W.

Anastasi. Naval Hospital Boston, Chelsea.

The purpose of this study is to perfect a method of stimulating bone growth electrically, especially with respect to bone deficiencies classified as cleft palate. One graft will be electrically stimulated by a placement of electrodes in the area of the bony defect. The graft of the opposite side will act as a control and will not be electrically stimulated. This research model is being constructed on 30 dogs. The purpose of this is to obviate the need for autogenous bone grafts to stabilize the bony palate.

Since Jul 1972, a new battery design has been made to deliver the best voltage and amperage to stimulate bone growth. Voltage and frequency rates have been established. Presently, modifications of the pulse durations and of current quantity are being tested in rats. Our studies with rat calvarium have shown us that with this newly designed battery we have successfully stimulated membranous bone growth.

M4305.05.01-3088

COMPOSITE TISSUE TRANSPLANTATION. D.H. McLean, G.A. LeBlanc and H. Buncke. Naval Hospital, Oakland and University of California, San Francisco.

The purpose of this study is to demonstrate the feasibility and advantages of partial limb and flap transfers in experimental animals. This is being accomplished through the use of microsurgery operative procedures. Studies involving rats have now been completed and for the past six months the investigators have successfully constructed an entire third ear from omentum, Silastic and split-skin grafts using a free omental transplant from the omentum to the head. It is planned to use omentum with split-thickness skin grafts for immediate cover of full-thickness scalp defects where split-thickness grafts alone would not survive due to the absence of adequate blood supply.

To date, the experiments have aided in clinical care of patients. Transplantation of omentum to fill a large scalp defect was successfully performed on a Navy enlisted man. Also, a successful transplantation of the right great toe, to replace a totally amputated right thumb was completed during the year.

During the next year work will continue on dogs and it is planned to anastomose the spermatic artery

to the superficial inferior epigastric artery, or an omental artery.

MR041.20.01-0241

THE USE OF PRESERVED COMPOSITE TENDON ALLOGRAFTS IN HAND SURGERY. W.D. Latham. Naval Hospital, Bethesda.

This project is designed to study the feasibility of storage and clinical use of freeze-dried tendon allografts in hand surgery.

No suitable candidates for the use of preserved freeze-dried flexor tendon allografts have presented themselves for treatment since the last report. Since these allografts are reserved for those patients in whom the standard methods of treatment for flexor-tendon deformities are not applicable, the number of potential candidates is expected to be small. Since there is no other good method of treating these severe problems it is felt that the investigation of the use of these allografts in suitable cases should be continued.

CICC 2-06-317

THE USE OF FREEZE-DRIED AURICULAR CARTILAGE ALLOGRAFTS IN EXTERNAL EAR CONSTRUCTION. W.D. Latham. Naval Hospital, Bethesda.

The aim of this study is to determine if freeze-dried auricular cartilage allografts can be used satisfactorily as auricular framework in reconstruction of the external ear.

Two patients are presently undergoing ear reconstruction with the use of cadaveric freeze-dried auricular cartilage allografts. Neither of these patients has completed their reconstruction. It has been determined that some absorption of the allograft auricular cartilage occurs and that it has been necessary to bolster the cadaveric auricular cartilage allograft with freeze-dried costal cartilage struts to provide adequately strong auricular framework.

The number of potential donors and recipients for these allografts is small, but the method shows some promise and the investigation should be continued.

CICC 2-06-314

SURGERY — THORACIC

THE BRONCHOFIBERSCOPE AS A NEW WEAPON IN DEALING WITH LUNG CANCER. B.L. Aaron and J.T. Mullen. Naval Hospital, Portsmouth, Va.

The purpose of this study is to determine whether the bronchofiberscope will be effective in rendering an earlier diagnosis of lung cancer than is now obtainable, and in establishing a diagnosis of cancer in inoperable patients. Suspicious lesions will be investigated to the maximum afforded by the bronchofiberscope, and in each one, brushings will be taken for cytology and cell block studies.

Only ten patients have been adequately evaluated for inclusion in the study to date. The yield so far has not been overly impressive with seven results consistent with the diagnosis (benign and malignant), three false negatives (all carcinoma), and no false positives. It is anticipated that confidence in the results will improve as experience with the scope is acquired.

CICC 3-08-083

CLINICAL EVALUATION OF IN-LINE FILTERS DURING EXTRACORPOREAL CIRCULATION. P. Ah-Tye and M. Hartley. Naval Hospital, San Diego.

In 18 dogs undergoing cardiopulmonary bypass for homograft valve replacement or aortocoronary vein bypass, Swank or Pall in-line filters were employed in the extracorporeal circuit. Studies of the circulating blood were undertaken at intervals. These included a control; 15 minutes on bypass; one hour on bypass, proximal and distal to the filter; and at the conclusion of bypass, proximal and distal to the filter. The studies included complete blood counts, platelet counts, fibrinogen levels, total proteins, total lipids, plasma hemoglobin, free fatty acids and osmotic fragility.

Evaluation of the data has not shown any significant changes upon which definitive conclusions could be drawn. More sophisticated measures such as screen-filtration pressures or ultra-sound determinations for microemboli may be necessary for a more meaningful study.

CICC 2-16-410

USE OF THE MEMBRANE LUNG AS A RESPIRATORY SUPPORT SYSTEM. P. Ah-Tye, M.J. O'Sullivan and C.L. Brodhead, Jr. Naval Hospital, San Diego.

Previously obtained Travenol 0.25 M² membrane oxygenators were employed in total cardiopulmonary bypass performed on five cats weighing from 3.75 kg

to 6.25 kg. The animals were supported on total bypass successfully for variable periods. Extreme hemodilution in these animals reached hematocrit levels of 11 and below. No homologous blood was available to afford survival in the immediate post-perfusion period. One large dog weighing 26 kg was supported by partial bypass, cannulating the femoral vein and femoral artery and employing the 0.75 M² Travenol membrane oxygenator. The animal was supported for two hours. There was difficulty in inducing a consistent pulmonary hypoxic condition. Further laboratory studies are contemplated in this area.

CICC 2-16-418

SEVERE HEMODILUTION TECHNIQUES FOR CARDIOPULMONARY BYPASS. R.G. Fosburg. Naval Hospital, San Diego.

Four adult mongrel dogs have been placed on cardiopulmonary bypass and, utilizing a dextrose-priming solution, severe hemodilution has been achieved to hematocrit levels of 6%. Several basic faults in the design of the original protocol have come to light. The first involves the need for splenectomy in the dog before undertaking this type of study. The second is related to pulmonary edema that results from severely reduced colloid osmotic pressure. Plasmapheresis may be required as well. No survivors have been observed. The logistic problem imposed by the lack of animal blood-banking procedures is also a factor in achieving resuscitation.

CICC 2-16-408

THE SIGNIFICANCE OF POSITIVE IPSILATERAL NODES IN RESECTIONS OF LUNG. R.G. Fosburg. Naval Hospital, San Diego.

Twenty patients have undergone anatomic and physiologic evaluations to assess the extent of involvement of carcinoma of the lung. All patients had mediastinoscopy and nine with positive ipsilateral nodes were subjected to extended radical pneumonectomy. There were four operative deaths. Of the remaining survivors, none lived beyond 14 months. Seven additional patients were explored and found to be unresectable. All survived beyond 11 months. The remaining four patients were not explored beyond mediastinoscopy: Two were judged to be poor operative risks; One developed a cervical metastasis before thoracotomy, and; The third received cobalt irradiation because of bony metastasis. He remains alive but with disease, at 23 months.

These results indicate a very ominous prognosis for positive ipsilateral nodal metastasis in carcinoma of the lung. Present policy is to regard these patients as inoperable despite the fact that the gross involvement can be excised by extended radical pneumonectomy. CICC 2-16-407

THE CONTENT OF PERICARDIAL FLUID: EFFECTS ON HEMOLYSIS DURING CARDIOPULMONARY BYPASS. R.G. Fosburg. Naval Hospital, San Diego.

The role of pericardial fluid in altering blood elements during cardiopulmonary bypass is studied in the laboratory animal and humans. Analysis of blood directly aspirated from the pericardium is compared to the perfusate after transit through the cardiectomy reservoir and oxygenator. Appropriate samples are analyzed for plasma hemoglobin, osmotic fragility, free fatty acids, total protein, fibrinogen, fibrin split products and platelets.

Work to date indicates an anticoagulant effect of pericardial fluid (fibrinolysin ?); however, too little information is present at the moment to make any definitive conclusions.

CICC 2-16-409

EVALUATION OF BRONCHIAL BRUSHING IN CHEST DIAGNOSIS. R.G. Fosburg. Naval Hospital, San Diego.

Twenty patients have been subjected to bronchial brushing under single-plane-image intensification. The brushes have been introduced through rigid bronchoscopes or preformed Rothene catheters. Diagnosis has been achieved by cytologic means in four patients who subsequently have undergone operations. Bacteriologic techniques have resulted in two additional diagnoses. This low yield is attributed to the lack of biplane-image intensification and the inability to perform selective subsegmental bronchus catheterization. Enhancement of results is anticipated when a fiberbronchoscope becomes available.

CICC 2-16-412

VASCULAR BYPASS EMPLOYING A HEPARINIZED POLYVINYL CHLORIDE CATHETER. R.G. Fosburg, P. Ah-Tye and M. Hartley. Naval Hospital, San Diego.

Resectional treatment of aneurysms of the thoracic aorta and its branches is an accepted surgical practice often performed with use of an extracorporeal circuit and systemic anticoagulation. This frequently results

in troublesome bleeding and difficulty with the integrity of suture lines due to paralysis of the clotting mechanism. The use of pre-heparinized bypass catheters offers an alternative method of treatment with significant advantages. During the period of report no operative candidate has been available for clinical use of these catheters.

CICC 3-16-049

THE INFLUENCE OF TRUNCAL SKIN REFLEXES ON AIRWAY RESISTANCE. R.G. Fosburg, D. Reid, P. Ah-Tye and J.A. Gibbons. Naval Hospital, San Diego.

This study will serve to identify the relation, if any, between airway dynamics and truncal skin reflexes. The counterirritant effect of various plasters applied to the chest will be explored. Ambient room temperatures (air-conditioned intensive care unit) with unclothed chests may influence airway resistance. Application of warmth to the trunk may improve airway resistance. Volunteers will be subjected to base-line assessment ventilatory functions. Then a variety of stimuli will be applied to the trunk, including: mustard plasters, heating pads, cooling pads, and cold-air currents directed across the skin.

CICC 3-16-051

OPTIMAL TIMING OF THORACOTOMY FOLLOWING BRONCHOGRAPHY. R.G. Fosburg, D. Reid and J.A. Gibbons. Naval Hospital, San Diego.

Static and dynamic lung volumes, airway resistance and diffusing capacities will be evaluated before, and at intervals after bronchography, to determine the response of the airways to radiographic contrast material. The influence of contrast agents on the bronchial mucosa can thus be determined and thoracotomy timed in relationship to the resolution of these effects.

CICC 3-16-035

OPTIMAL TIMING OF BILATERAL THORACOTOMY. R.G. Fosburg, D. Reid and M.J. O'Sullivan. Naval Hospital, San Diego.

Spontaneous pneumothorax has the highest incidence during the second and third decades of life and is an important cause of morbidity in military personnel. Bilateral occurrences are frequently managed by pleural abrasion. The appropriate time interval between procedures requires definition and the impact of a program of vigorous physical therapy might significantly alter that interval. Through measurement of ventilatory-

function studies and serial determinations of inspiratory and expiratory girth, it would be possible to document the recovery rate and ascertain when a subsequent thoracotomy could be more safely performed. During the period of report no work has been accomplished on this project.

CICC 3-16-027

EVALUATION OF TREATMENT OF PULMONARY DYSFUNCTION FOLLOWING HEMORRHAGIC SHOCK. R.G. Fosburg and R.W. Virgilio. Naval Hospital, San Diego.

The objective of this study is to identify parameters of respiratory mechanics and gas exchange which will preclude the development of posttraumatic pulmonary insufficiency and pulmonary dysfunction following hemorrhagic shock. A respiratory cart has been developed which permits on-line computerized analysis via telephone lines to a remote computer. During the past year, 115 patients have been admitted to the Shock Research Unit and extensively studied. The analog data obtained from pressure transducers, green-dye curves, and airway dynamics have been recorded on tape. The tape has then been hand-carried to a computer at the University of California, San Diego, where it has been analyzed. This work has permitted calibration of all equipment and development of a data-acquisition sequence compatible with the computer. Hard copy has then been brought back for analysis.

At present one digital telephone line for duplex communication between the special bedside respiratory cart and the Patient Monitoring Computer has been installed. The two FM dial-up telephone lines will be installed in early 1973. On-line operation is anticipated shortly thereafter. This will provide the first Naval Hospital computerized-monitoring capability for critically ill patients.

MR041.20.01-0289

RESECTION OF PULMONARY SECONDARY TUMORS. D.E. Hutchison and R.M. Deaner. Naval Hospital, Oakland.

Under various circumstances, 21 patients underwent pulmonary resection for metastatic disease at Nav Hosp Oakland during the period 1960-1971. Surgical therapy for metastatic neoplasms of the lung is directed by several specific factors. Acceptable criteria for resection are as follows: 1) identifiable and resectable pulmonary lesion(s); 2) metastasis to no other organ; 3) controlled primary lesion; and 4) significant disease-free interval. Excellent results (30% and 40% five-year

survival) have been recorded when these principles were strictly adhered to. Relaxing of these criteria has also occasionally led to encouraging success. Little can be said regarding the resected secondary lesion when the primary lesion is unidentified or undiscovered. Results are often dismal unless the primary tumor is quickly uncovered and controlled.

CICC 2-48-201

MANAGEMENT OF RESPIRATORY INSUFFICIENCY WITH A MEMBRANE OXYGENATOR. M. Mills, B. Shepard and H. Ashworth. Naval Hospital, Bethesda.

Long-term partial bypass in sheep and two humans was discouraging because of bleeding and difficulties with the extracorporeal circuit. We therefore turned to total bypass in dogs and have done six three-hour perfusions with no survivors. Three of the deaths were due to carbon dioxide retention. The others were due to defects in the extracorporeal circuit. When we are able to get survivors in animals, we will use a membrane lung for selected clinical open-heart cases. We feel this is necessary to gain the technical expertise to be able to use a membrane lung in an emergency. We are also beginning work on a non-thrombogenic extracorporeal circuit to decrease the need for heparin. Use of membrane lung support in combat casualties is not likely to be successful until this can be accomplished. M4305.05-3039

DEVELOPMENT OF A PORTABLE VOLUME-CONTROLLED RESPIRATOR. M. Mills. Naval Hospital, Bethesda.

The advanced development prototypes of the portable volume-controlled respirator (PVCr) have been used for 2040 hours on 165 patients. This includes 305 hours of closed-cycle operation. Ten respiratory failure cases have been successfully transported using closed-cycle and battery power for up to four hours. Comparative tests with five commercially available ventilators (Ohio 560, Bennett MA-1, Engstrom, Emerson and AirShields) have shown our machine to have equal or superior performance. Design specifications for the engineering prototype have been written and circulated to the three military services for review. A final contract with General Electric is planned. It will result in a ventilator which meets military specifications for environment and stress, and which has a degree of reliability and safety not previously available.

M4305.05-3027

SAPHENOUS VEIN GRAFTING IN CORONARY RE-VASCULARIZATION. J.H. Oury and C.L. Brodhead, Jr. Naval Hospital, San Diego.

Twenty-one mongrel dogs have undergone ascending aorta to left anterior descending cardiopulmonary bypass. Fourteen allograft jugular veins, ten processed in Hanks solution and four freeze dried and irradiated, plus seven autogenous forepaw veins have been utilized. Twelve animals surviving from two days to 2½ months have undergone postoperative coronary arteriography. The vein-coronary anastomoses were occluded in all twelve animals. Histologic sections have failed to reveal rejection as a causal mechanism.

It is postulated that technical difficulties or collateralization to the coronary system has altered runoff and lead to thrombosis on the basis of stasis. Additional animals will be prepared using ameroid constrictors to reproduce chronic ischemia, in hopes that subsequent vein-bypass grafting can be performed, thus continuing the inquiry into the feasibility of allograft veins.

Clinically, 22 patients have undergone similar operations employing autogenous saphenous veins; of 18 survivors, eight have undergone subsequent cardiac catheterization and exercise testing. Improved ventricular performance and relief of angina pectoris has occurred in all. The efficacy of the surgical approach to coronary artery disease is attaining increased recognition. The possibility of a homograft vein bank still warrants continued investigation.

CICC 2-16-402

AN EVALUATION OF TISSUE PRESERVATION TECHNIQUES RELATED TO AORTIC HOMOGRAFT VALVES. J.H. Oury, M.J. O'Sullivan and J.W. Hammon, Jr. Naval Hospital, San Diego.

To study allograft aortic valves mounted in the mitral position and to determine the ideal method of procurement and preservation, mitral valves were replaced in a series of animals, using an allograft mounted on a titanium frame. The allograft was procured from a fresh specimen and used within 24 hours. A second group received allografts which had been preserved for three months by quick-freezing preservation. The valves were quick frozen in a controlled fashion, at the rate of 1° C per minute, to a temperature of -40° C. They were then stored in vapor phase of liquid nitrogen for three to four months, at which time they were defrosted rapidly, cultured and reimplanted as allograft valves in the mitral position.

We have found that no appreciable level of cytotoxic antibody could be demonstrated. This group of animals has been sacrificed and their valves have been examined by electron microscopy.
M4305.05-3074

MECHANISMS OF TERMINAL AIRWAY CLOSURE ASSOCIATED WITH CARDIOPULMONARY BYPASS. D. Reid, A.D. Hagan, R.G. Fosburg and M. Hartley. Naval Hospital, San Diego.

It is well known that patients undergoing cardiopulmonary bypass demonstrate arterial desaturation upon the cessation of bypass. This effect is related to arterial flow rates and preexisting cardiopulmonary pathology. It is felt by many investigators that the mechanism for the pulmonary pathology is terminal airway closure; however, the mechanism for their closure is unclear.

All patients undergoing cardiac bypass for open-heart surgery will constitute the study population. A look at the many known causative factors for terminal airway closure will be accomplished. This will include terminal airway CO₂ tension, histamine and serotonin concentrations of plasma and surfactant measurement of minced lung specimens. The patient population is expected to include 50 patients.

Initiation of this project has been delayed pending solution of mechanical problems as related to the study. Attempts are presently being made to establish the model structure of the protocol.
CICC 3-16-050

EVALUATION OF PREVIOUSLY FROZEN RED BLOOD CELLS IN EXTRACORPOREAL CIRCULATION FOR TREATMENT OF LESIONS OF THE HEART AND GREAT VESSELS. B.M. Shepard, M. Mills and H.E. Ashworth. Naval Hospital, Bethesda.

It is the purpose of this study to examine the behavior of thawed, previously frozen red blood cells when used to prime the pump-oxygenator and replace blood loss during extracorporeal circulation for cardiovascular surgery. The results will be compared to the activity of fresh liquid preserved blood to be used in an identical system. If frozen red cells are found to perform with equal efficiency and produce no more complications than fresh blood, clinical use can be made of freeze preservation, which presents a number of advantages. These include: avoidance of the hepatitis problem; decrease in the micro-debris found in conventionally banked blood; virtual elimination of blood incompatibility problems; provision for patients

to store their own red cells for elective surgery; and provision for storage of large quantities of blood in anticipation of sudden, unexpected demands on limited quantities of fresh whole blood.

During the period of this report, four animals have been studied, using fresh whole blood in two and using thawed, previously frozen red cells in two animals. The early results indicate that previously frozen red cells compare favorably with fresh whole blood, that the design of the experiment is satisfactory, and that extension of the study to clinical application is justified.

CICC 3-06-193

THE RECOVERY OF VENTILATION-PERFUSION (V/Q) FOLLOWING PNEUMOTHORAX. W.J. Storz. Naval Hospital, San Diego.

The time course of the return of ventilation and perfusion (V/Q) after reexpansion of the lung, following a pneumothorax is being investigated utilizing xenon scintiphotographic scanning.

One patient studied to date demonstrates prompt recovery of V/Q, although the necessity to have the study performed at another hospital has introduced a significant time delay. Two additional patients were entered into the protocol but efforts to complete the study had to be aborted because of unavailability of the Anger camera. The capability to perform these studies in-house is about to materialize. The Anger camera has been married with the computer and a program is being evolved for compartmentalization of the lung field.

CICC 2-16-414

PREDICTION OF THE RESULTS OF CARDIAC SURGERY BY THE USE OF AN ACCEPTANCE SCALE. J.D. Vincer, M. Mills and D. Mimbs. NMMC, Bethesda.

This clinical investigation will attempt to correlate the results of cardiac surgery as measured by the NYHA classification and the degree of acceptance on the part of the patient as measured by an acceptance scale developed by the team of Mason, Clark, Reeves and Wagner of the Columbia Presbyterian Hospital, N.Y. (*Journal of Religion and Health*, 8:2, Apr 1969). The results of cardiac surgery, as stated by the investigative hypothesis are determined by the degree of acceptance of the total surgical process. In this process each patient is rated at least 24 hours prior to surgery, during routine preoperative visits, and is unaware that he is being rated. The raters are selected in designated numbers from the staff of chaplains, nurses,

cardiologists, and corpsmen who have been trained in the use of the acceptance scale.

Over the span of the first 50 patients rated, the scale has been validated as a scientific measurement. The statistical coefficient reported by each of the raters was less than .001 of significance (so much less that the X^2 table doesn't extend that far!). Phase II of the research design focuses on a therapeutic approach to raise the acceptance level of apparent non-accepting patients.

CICC 2-06-302

UROLOGY

TESTICULAR TUMORS — A STUDY OF MULLERIAN-INHIBITING SUBSTANCE. N.L. Constantinople and M.B. Rotner. Naval Hospital, San Diego.

During fetal life, the testis produces a nondialyzable, nonsteroidal substance which causes regression of Müller's ducts. Because testicular tumors arise from embryonic elements and are known to produce other hormones, an assay system has been employed to determine the presence of Mullerian-inhibiting substance (MIS) in testicular tumors.

Explants of testicular tumors are incubated with 14-day-old fetal rat Mullerian ducts in organ culture. The production of MIS is documented by histologic regression of the Mullerian ducts after three days of incubation. Fetal rat, dog and human testes have also been incubated to demonstrate regression *in vitro*.

To date, numerous fetal dissections have isolated over 50 duct systems which have been incubated with: three human testicular tumors (one teratocarcinoma, one embryonal-cell carcinoma and one seminoma); over 20 fetal rat testes; and 5 fetal canine testes. So far, we have demonstrated tumor regression and no reproducible regression with fetal testes. Further dissections with refinement in technique are now in progress. No valid conclusions can be inferred at this time.

CICC 2-16-403

ILEOCYSTOPLASTY UTILIZING A MUCOSA-FREE ILEAL SEGMENT. P.M. Crum and E. Baran. Naval Hospital, Portsmouth, Va.

This study is being conducted to evaluate the feasibility of utilizing mucosa-free ileum to eliminate the usual complications of hyperchloremia and mucous secretion in the standard ileocystoplasty procedure.

Eighty percent of the normal dog bladder has been

removed, and a segment of ileum has been isolated and fashioned for anastomosis to the residual bladder base. Mucosal and submucosal elements have been stripped from the ileal segment in an attempt to reduce chloride absorption and mucous secretion. Animals have been studied periodically with urinalyses, urine cultures, excretory urography, cystography, cystometry and blood chemistries, and have ultimately been sacrificed 14 weeks after ileocystoplasty.

Initial data suggest that a functionally satisfactory bladder has been obtained, and no mucous secretion or hyperchloremia has occurred. Re-epithelialization of the denuded ileal segment with transitional-cell epithelium has been consistently observed. The study is still in progress at the time of this report.

MR041.20.01-0396

SUPRAPUBIC BLADDER DECOMPRESSION FOR URINARY RETENTION IN POSTOPERATIVE PATIENTS USING TWELVE-GAUGE INTERCATH. W.J. Fouty. Naval Hospital, Bethesda.

It is theorized the incidence of urinary-tract infection is decreased when a method of suprapubic bladder decompression is used.

The number of patients studied thus far is insignificant for conclusions. However, it is apparent that there will be a decreased infection rate, using the suprapubic method as compared with routine catheterization. It is hoped this study will prove the method to be effective and safe for postoperative urinary-bladder decompression.

CICC 2-06-320

DIAGNOSIS AND TREATMENT OF CALCIUM OXALATE UROLITHIASIS. M.H. Humphreys and J.E. Keeton. Naval Hospital, Great Lakes.

Calcium oxalate urolithiasis is a common and troublesome occurrence, and is found in a variety of clinical settings. The bulk of patients with this disorder are felt primarily to have disorders of calcium metabolism; on the other hand, a number of such patients may have either primary or secondary disorders of oxalate metabolism. The present study was designed to examine this latter group of patients. However, no patients with either primary, or secondary disorders of oxalate metabolism, and consequent urolithiasis, have been found for study up to the present time.

CICC 3-13-138

DIAGNOSIS OF URINARY-TRACT OBSTRUCTION BY SCINTIPHOTOGRAPHY. G.J. Weir, Jr. Naval Hospital, Great Lakes.

Eight patients with clinical histories suggestive of urinary-tract obstruction were studied. Renal isotopic studies agree with intravenous pyelography (IVP) findings in six patients. One patient, who had a past history of stone and recent onset of renal colic, showed no obstruction by renography. The patient was allergic to dye and no IVP was performed. Clinically he did well with no evidence of obstruction. One renogram, in a patient with epididymitis was falsely interpreted as positive for generalized obstruction. Five other patients, studied for reasons other than obstruction, showed persistent localized areas of isotope concentration. Two of these were located in the renal area: one at the renal pelvis, and two along the ureter. These localized areas are apparently without clinical importance.

CICC 2-13-017

DYNAMIC SCINTIPHOTOGRAPHY IN THE EVALUATION OF RENAL DISEASE. G.J. Weir, Jr. Naval Hospital, Great Lakes.

This study was designed to assess the value of dynamic scintiphotography, using a variety of radio-

pharmaceuticals, in renal disease. Eight-mm movie films were prepared of ^{99m}Tc technetium pertechnetate (^{99m}Tc), ^{131}I -hippuran, and ^{99m}Tc -DTPA images for varying periods following injection. The size of these images and the delay in getting them developed have presented an insurmountable obstacle in developing this as a diagnostic aid. Images on Polaroid film have proven of some use.

Eighteen patients were studied. In seven cases the scintigraphic work positively influenced patient management; in six it had no effect; and in five instances it helped stimulate more invasive diagnostic procedures with an eventual diagnosis of normal, or inconsequential anatomical variation. It is believed that these latter instances partially reflected a learning process and that they should diminish in the future. In eight cases the scintigraphic work confirmed lesions demonstrated on intravenous pyelography (IVP). In two cases it helped the urologist to plan surgery, by substantiating the existence of residual function not indicated by IVP.

Four patients had IVPs which were equivocally suggestive of a mass lesion. Three of these had normal renograms/renal scintigraphy and were not evaluated further. One had a mass lesion by scintigram, which proved to represent a duplicated collecting system causing ureteral obstruction.

CICC 2-13-018

COVER PHOTOGRAPHS (by Edward Moore)

We are indebted to our Gastroenterology Editor, CAPT D.O. Castell, MC, USN for providing timely photos appearing on the front and back covers. As Chief, Clinical Investigation Service at Naval Hospital Philadelphia, Pa., CAPT Castell has selected representative views of Clinical Investigation Center activities which flourish at Nav Hosp Philadelphia. Participants are identified as follows:

Front Cover

Upper left — CAPT A.R. Chappelka, MC, USN performs subculture studies of bowel microflora.

Lower left — HM2 P. Jasis, USN is seen at work in the radioisotope laboratory.

Upper right — CAPT R.A. Burningham, MC, USN conducts study of leukemia survival in mice.

Lower right — LCDR J.H. Dunne, MC, USNR (in cooperation with HARVEY) is working on antibody formation in a rabbit model.

Back Cover

Left — CDR D.N. Pasquale, MC, USN is conducting blood coagulation studies.

Upper right — Ada M. Lin, Ph.D., conducts spectrophotometric enzyme determination.

Lower right — LCDR J.P. Kirchner, MC, USNR prepares tissue specimen for electron microscopy.

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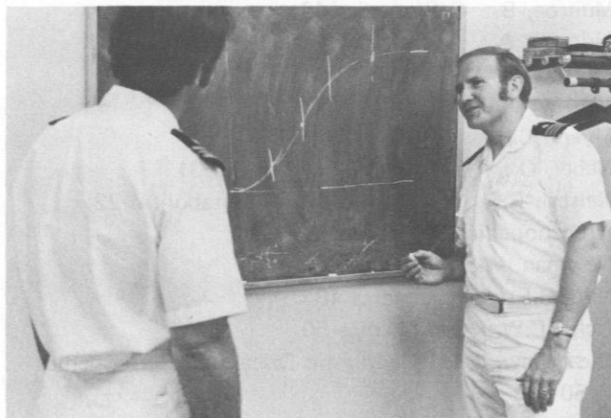
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THINK CHEESE.—Staff members at Nav Hosp Philadelphia, engaged in Clinical Investigation Service studies of the gastric mucosal barrier, are LCDR G.L. Eastwood, MC, USNR and Janet Gray (left). They are pictured while intubating a calm and reassured little mouse.



RUN THAT BY ME AGAIN.—Chief of the Clinical Investigation Service at Nav Hosp Philadelphia, CAPT D.O. Castell, MC, USN (right), discusses experimental data with LCDR R.H. Higgs, MC, USNR (left).

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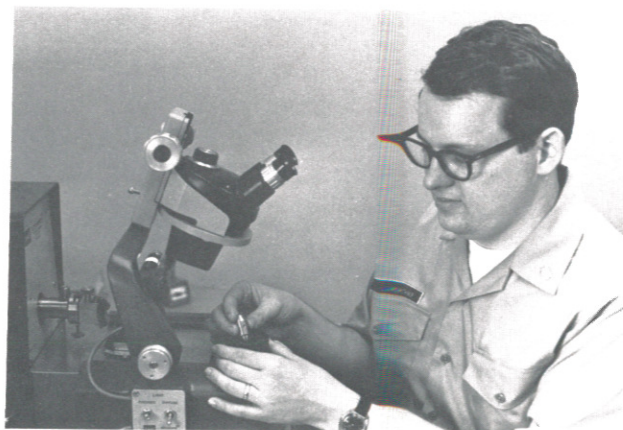
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